Case Report

A retrobulbar meningioma as a cause of unilateral exophthalmos and blindness in a horse

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Summary

This report describes the unusual diagnosis of a retrobulbar syncytial meningioma in a 16-year-old Thoroughbred gelding. The horse initially presented with unilateral left sided exophthalmos and apparent blindness characterised by unilaterally absent menace and pupillary light responses. Magnetic resonance imaging (MRI) identified a well-defined soft tissue mass intimately associated with the optic nerve. Based on the characteristic MRI appearance, a meningioma was suspected. The eye was enucleated under general anaesthesia and partial excision of the mass was achieved. Histopathology confirmed the diagnosis and the horse underwent a course of adjuvant radiotherapy. Twelve months following surgery the horse is back in work, no neurological abnormalities have been detected and follow-up computed tomographic imaging of the skull has revealed mild bone sclerosis with no remnants of the mass identified.

Introduction

Exophthalmos is an acquired displacement of the globe due to an increase of orbital contents (Baujat et al. 2006). This is usually the result of a retrobulbar mass displacing the globe rostrally. Previously described retrobulbar masses in the horse include abscesses, haematomas, a dermoid cyst and a hydatid cyst (Barnett et al. 1988; Reilly et al. 1994; Hubert et al. 1996; Munoz et al. 2007). Primary retrobulbar lesions in the horse are less commonly reported than extension of disease from local structures, such as the paranasal sinuses or the ethmoid turbinate bones. Disease processes that have been described include neoplasia such as adenocarcinoma, osteoma or cementoma of the frontal sinus, progressive ethmoid haematoma and sinonasal cysts (Hill et al. 1989; Davis et al. 2002; Scotty et al. 2004; Schaaf et al. 2007; Annear et al. 2008). Infectious processes include meningitis, pituitary abscesses and cryptococcus infection of the frontal sinus (Scott et al. 1974). Traumatic and degenerative diseases such as skull fractures and myonecrosis of the muscles of mastication also occur (Caron et al. 1986; Step et al. 1991).

Primary neoplasms identified in the retrobulbar space of the horse are very rare. Isolated case reports include neuroendocrine tumours, neuroepithelial tumours of the retina and optic nerve, malignant lymphoma and microglioma (Lavach and Severin 1977; Eagle et al. 1978; Bistner et al. 1983; Basher et al. 1997; Dopke et al. 2005; Sharma et al. 2005). The close association of these tumours with the optic nerve often results in unilateral blindness, and they may be locally invasive, resulting in intracranial spread or metastasis.

This case report describes the presentation, diagnosis and treatment of a retrobulbar syncytial meningioma, which to the authors’ knowledge has not previously been reported in the horse.

Case details

History

A 16-year-old Thoroughbred gelding presented to the Royal Veterinary College Equine Referral Hospital with a 3 week history of exophthalmos affecting the left eye. The owner had first noticed a mild serous ocular discharge that gradually progressed over several days to protrusion of the globe. Subsequently the horse had become increasingly startled when approached from the left side. The eye had been treated for suspected glaucoma with phenylbutazone (Equipalazone)1 (2.2 mg/kg bwt per os b.i.d.) and topical timolol maleate/dorzolamide (Cosopt)2 t.i.d., with no apparent improvement.

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Physical examination

The horse was bright, alert, responsive and in good body condition; vital parameters were within normal limits. Moderate exophthalmos affecting the left globe was noted (Fig 1). The left pupil was markedly dilated. The left direct and the left consensual pupillary light responses, the left dazzle response and the left sided menace response were absent but all reflexes were present in the right eye. Corneal and palpebral reflexes were present bilaterally. Evaluation of the other cranial nerves identified no deficits.

Ophthalmological examination

Bilateral local analgesia of the auriculopalpebral nerves was performed using 1 ml mepivacaine (Intra-Epicaine)1. Evaluation of the right eye identified no abnormalities. Fundic examination via direct ophthalmoscopy revealed no clinically significant abnormalities in either eye. The intraocular pressure was close to the upper level of the normal range in both eyes (left eye: 37 mmHg; right eye: 34 mmHg; reference range 16–36 mmHg).

Diagnosis

Ultrasonography

Transpalpebral ultrasonography, performed using a 12 MHz linear probe, identified a similar globe size in both eyes (Fig 2). Transverse cross-sectional measurements of the left eye were 40.3 x 44.8 mm and 38.2 x 45.6 mm in the right eye. No retrobulbar mass could be identified. In light of the normal intraocular pressures and ultrasonographic appearance of the globe in conjunction with the strong clinical suspicion of a retrobulbar mass, further diagnostic imaging in the form of magnetic resonance imaging (MRI) was performed.

Magnetic resonance imaging

Magnetic resonance imaging was performed at the Animal Health Trust with the horse in right lateral recumbency under general anaesthesia, using a short-bore Signa Echospeed3 1.5 T magnet. Transverse, dorsal and sagittal T1 and T2 weighted fast spin echo (FSE) sequences were obtained with a 5 mm slice thickness, in addition to transverse T2 gradient echo and T1 weighted fat suppressed FSE sequences after injection of contrast agent (gadolinium, 20 ml i.v.; Multihance)4. There was rostral, dorsal and lateral displacement of the left eye by a well-defined, ovoid soft tissue mass within the orbit, which displaced the extraocular muscles between the mass and globe. There was no osseous pathology. The mass was approximately 3 cm in diameter and 6 cm in length in a rostrocaudal direction and extended caudally into the orbit apex, tapering caudally (Figs 3a and b). The mass was intimately associated with the optic nerve, although there was no involvement at the level of the optic chiasm, and hyperintense to muscle in both T1 and T2 weighted FSE images. There was intense, homogenous signal enhancement after administration of gadolinium (Fig 3c), with no abnormal meningeal enhancement inside the calvarium. The MRI appearance of the mass, characterised by its discrete nature, avid contrast enhancement, tapering caudal margin and intimate association with the optic nerve, was strongly suggestive of a meningioma involving the left optic nerve, which resulted in protrusion of the globe.

Treatment

Based on reports from other species (Mauldin et al. 2000; Turbin et al. 2002) it was decided to remove the accessible part of the tumour. Complete excision is rarely possible because of the close association of the tumour with the optic nerve; therefore subsequent radiation therapy was recommended to maximise the chances of therapeutic success.

Enucleation

The horse received oral flunixin meglumine (Finadyne)5 (1.1 mg/kg bwt b.i.d.) and perioperative antimicrobial drugs consisting of procaine penicillin (Norocillin)6 (22,000iu/kg bwt i.m. b.i.d.) and gentamicin sulphate (Genta-Kel)7 (6.6 mg/kg bwt i.v. s.i.d.). Intravenous morphine sulphate8 (0.1 mg/kg bwt) was added for additional perioperative analgesia. The left eye was enucleated under general anaesthesia via a transpalpebral approach (Brooks 2006). The intraorbital portion of the retrobulbar mass was debulked; however, as expected from the MR images, complete excision was not possible due to deeper attachments and the proximity to vital structures. Due to significant intraoperative haemorrhage a transfusion of 9 l of whole blood was administered. The orbit was packed with sterile gauzes and...
a head bandage applied. Post operative management consisted of a further 5 days of antimicrobial treatment and flunixin meglumine. The horse returned to normal management with no further signs of discomfort or neurological deficits.

**Histology**

The mass was lobulated and organised into lobes and nests rimmed by flattened cells, which were supported by broad trabeculae of dense fibrous stroma (Fig 4a). There were polygonal neoplastic cells with moderate amounts of pale eosinophilic and slightly granular cytoplasm, with indistinct margins (Fig 4b). Nuclei were round with stippled chromatin and moderate anisokaryosis. The optic nerve was surrounded by fibrous tissue, with apparent constriction and loss of normal structure in conjunction with prominent ballooning of the myelin sheath. The neoplastic tissue extended beyond the margins of the tissue specimen. These findings were consistent with a retrobulbar syncytial meningioma.

**Radiation therapy**

Three weeks after surgery, to allow for the surgical site to heal, the horse received a course of megavoltage radiation treatment at Cambridge University Veterinary School, under general anaesthesia. Four 800 cGy fractions of 6 MeV photon radiation were administered via 2 perpendicular fields (left lateral and dorsoventral) via a linear accelerator (ClinAc DMX) at one week intervals. Due to the frequency of therapy and the cost of transportation, the horse remained hospitalised between treatments. Phenylbutazone (2.2 mg/kg bw i.v. b.i.d.) was
administered as required to reduce any inflammation occurring secondary to the treatment. Radiation therapy was tolerated well and no complications were encountered. Slight scaling and erythema of the overlying skin and one episode of discomfort after one of the therapy sessions resolved without treatment.

Twelve months after treatment, the horse had returned to work as a general riding horse and clinical examination revealed no neurological deficits. A standing CT examination of the head was performed to identify any remnant or regrowth of the tumour. MRI had been recommended to the owners; however, this was declined for financial reasons and the requirement to anaesthetise the horse. There was mild sclerosis of the underlying bone, although no lysis was identified. Although it is less sensitive than MRI for differentiating soft tissue lesions, no mass effect could be detected on the CT images.

Discussion

Neoplasia of the optic nerve and sheath occurs uncommonly in man and domestic animals (Mauldin et al. 2000; Eddleman and Liu 2007). Optic nerve sheath meningiomas (ONSM) account for only 2% of all orbital tumours in man and constitute one-third of all tumours that affect the optic nerve (Saeed et al. 2003; Eddleman and Liu 2007). Benign gliomas are the most frequently occurring tumours of the optic nerve, whilst meningiomas are the most commonly occurring tumours that affect the optic nerve sheath (Miller 2004). Meningiomas are more commonly seen affecting the brain or the spinal cord, with only 1–2% of all those reported being optic nerve sheath meningiomas (Saeed et al. 2003; Montoliu et al. 2006). Those meningiomas that arise from the optic nerve sheath have distinct morphological features including myxoid, cartilaginous and osseous metaplasia and it has been suggested that they should be considered as separate entities to other meningiomas (Montoliu et al. 2006).

Meningiomas are slow growing indolent tumours with benign characteristics, although individual case reports of more aggressive tumour behaviour and pulmonary metastases have been reported in man (Mauldin et al. 2000; Perry et al. 2001; Miller 2004). Usually the tumour grows along the optic nerves in the subdural space and its local expansion is limited by the dural space, therefore they tend not to invade locally (Miller 2004). Syncytial meningiomas occur when there is cytoplasmic continuity between cells. Human ONSM have been reported to affect all ages and sexes, although middle-aged women are over-represented (Dutton 1991). In other species no sex predilection has been identified although some dog breeds, such as German Shepherds, Collies, Terriers and Poodles are over represented (Montoliu et al. 2006). To the authors’ knowledge an ONSM has not previously been reported in the horse.

A diagnosis of ONSM is often suspected on the basis of patient history, ophthalmological examination and advanced diagnostic imaging. Human patients with ONSM present with slowly progressive loss of vision and proptosis (Dutton 1991; Miller 2004). Fundic examination may reveal a pale or swollen optic disc but, in many cases, such as the horse described, the optic disc may appear...
normal. Both MRI and CT have been used to aid diagnosis of these tumours in human medicine. Typical findings are tubular enlargement of the optic nerve with bulbous enlargement at the nerve apex. Mineralisation surrounding the nerve has been reported in 20–50% of cases, along with homogeneous enhancement with gadolinium (Mafee et al. 1999). MRI is the imaging modality of choice because of superior soft tissue definition. Human meningiomas have isointense or hypointense signal relative to brain parenchyma on T1 weighted images and hyperintense signal on T2 weighted scans (Mafee et al. 1999). However, in the horse described, the tumour had similar signal intensity to the brain parenchyma in T2 weighted images (Figs 3a and b). The use of gadolinium contrast resulted in better definition of the margins of the tumour (Kuriashkin and Losonsky 2000). The anatomical detail provided by the MR images enabled accurate planning of the required surgical approach. It was clear that resection of the entire mass would not be feasible and that radiation therapy would also be required. The MR images were essential for generating the radiation therapy treatment plan. The ability to visualise the close proximity of the mass to other vital structures suggested preoperatively the need for adjunctive therapy and highlighted the risk of bleeding before the procedure.

The prognosis associated with optic nerve sheath meningiomas in human patients is very good, using a combination of radiotherapy with or without surgical debriodment. In 2 studies, which followed patients for a median time of 2 and 3 years, respectively, there was no recurrence of tumour growth detected on MRI (Andrews et al. 2002; Becker et al. 2002). In a longer study, which followed 64 patients for a median duration of 150 months, 8/64 patients showed radiographic progression following surgical resection and radiotherapy (Turbin et al. 2002). Therefore, we would expect the likelihood of tumour recurrence in the horse described in this report to be very small. However, as the current follow-up time is very short, it is possible that it is too soon to detect tumour recurrence.

Radiotherapy is the treatment of choice for human ONSMs, where the primary aim of treatment is to preserve vision (Miller 2002a,b; Wilhelm 2009). This therapy is preferred due to the low likelihood of these tumours to...
spread locally and cause neurological signs and the high complication rate associated with surgical treatment (Egan and Lessell 2002; Turbin et al. 2002). Radiation therapy acts by ionising cellular macromolecules that directly damage DNA; it indirectly interacts with nearby water molecules inducing apoptosis. Normal cells are able to repair this damage whilst tumour cells are not. There are 2 main ways in which radiotherapy may be administered; teletherapy involves a linear accelerator at some distance from the patient which achieves good tissue penetration; and brachytherapy involves the application of a sealed radioactive source directly to the tumour and minimises the damage to local tissues. Brachytherapy may involve intralesional implants such as iridium wires or administration of the radiation across the tissue surface, known as plesiotherapy (Theon 1998).

Interstitial implants are more commonly used for superficial tumours in the horse such as sarcoids and periorcular squamous cell carcinoma (Theon and Pascoe 1995; Byam-Cook et al. 2006). In one study of 157 cases of ocular and adnexal squamous cell carcinomas, treatment with strontium 90 reduced the overall recurrence rate from 44% to 11%, significantly reducing the incidence of tumour regrowth at the limbus, cornea, eyelids and bulbar conjunctiva (Mosunic et al. 2004). This study also included one horse with a tumour affecting the third eyelid which received cobalt teletherapy. Megavoltage teletherapy is performed much less frequently in the horse due to the small number of treatment facilities, the cost of treatment and the requirement to undergo multiple general anaesthetics. Therapeutic indications of megavoltage teletherapy in the horse include small inaccessible tumours or large radiosensitive tumours of the head and extremities. There are only a few published reports of megavoltage teletherapy in the horse including the successful treatment of 2 horses with ossifying fibroma affecting the mandible and paranasal sinuses, 3 horses with squamous cell carcinoma of the nasal cavity and sinuses and 4 horses with lymphoma affecting the head, perineum and hock (Robbins et al. 1996; Walker et al. 1998; Henson et al. 2004; Mosunic et al. 2004; Orsini et al. 2004). As demonstrated by the horse described, radiotherapy is a good therapeutic option for tumours such as squamous cell carcinoma, ossifying fibroma or meningioma located in inaccessible areas or adjacent to vital structures, such as the jaw, nasal cavity, sinuses or retrobulbar region in the horse.

The combination of radiation therapy with a conservative surgical approach aims to limit the number of tumour cells via debulking and improve the functional and cosmetic results compared with more aggressive surgery. Sufficient data are lacking in equine patients; however, in one study of human patients with ONSM, 92% retained vision and 42% had improved vision up to 284 weeks following radiotherapy alone (Andrews et al. 2002). Ocular complications resulting from focal radiotherapy have included the induction of optic neuropathies, retinopathy, dry eyes and cataract formation (Durkin et al. 2007). In the horse described, the eye was enucleated to allow debulking of the lesion and histopathological confirmation of the diagnosis, so there were no potential ocular side effects.

Chemotherapeutic agents have been utilised in the treatment of nonresectable meningiomas in man, the most common being hydroxyurea. (Schrell et al. 1997; Paus et al. 2003; Newton et al. 2004). Hydroxyurea reduces the production of deoxyribonucleotides via inhibition of the enzyme ribonucleotide reductase. The use of hydroxyurea in human patients has been associated with myelosuppression, dermatological reactions and hepatopathy (Mason et al. 2002). Hydroxyurea has been used experimentally with dexamethasone to treat a horse with multi-systemic eosinophilic epitheliotropic disease (Hillyer and Mair 1992) and a dog with a meningioma of the base of the skull (Tamura et al. 2007). In both cases a transient clinical improvement was observed. Larger controlled studies are required to evaluate the use of hydroxyurea in the horse.

The horse presented here highlights that ONSM should be included as differential diagnosis for any horse presenting with signs of exophthalmos and blindness. Ophthalmological evaluation may identify changes of the optic nerve; however, fundic examination may be unremarkable. MRI is the diagnostic imaging modality of choice and characteristic findings can be highly suggestive of the diagnosis, but this can only be confirmed by histopathological examination of tumour tissue, which requires enucleation. Due to the close proximity of the tumours to vital neural tissue complete excision is often not possible and in these cases radiotherapy may be the adjunctive treatment of choice. With such treatment the prognosis for survival, with unilateral loss of vision, is good.

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Manufacturers’ addresses

1Dechra Veterinary Products, Hatfield, Shrewsbury, Shropshire, UK.
2Merck Sharp and Dohme, Cramlington, Northumberland, UK.
3General Electric, Milwaukee, Wisconsin, USA.
4Bracco s.p.a., Milan, Italy.
5Intervet/Schering-Plough Animal Health, Walton, Milton Keynes, Buckinghamshire, UK.
6Norbrook Laboratories, Newry, County Down, UK.
7Kela NV, Hoogstraten, Belgium.
8Morphine, Martindale pharmaceuticals, Romford, Essex, UK.
9Varian, Palo Alto, California, USA.

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