

## Case Report

**Spinal ataxia in a 2-year-old colt caused by a compressive primary vertebral osteosarcoma****N. Fouche<sup>†\*</sup>, S. Oesch<sup>†</sup>, L. Unger<sup>†</sup>, I. Berenguer Veiga<sup>‡</sup>, L. Kuchler<sup>‡</sup>, M. Molazem<sup>§</sup> and E. Van der Vekens<sup>§</sup>**<sup>†</sup>Swiss Institute of Equine Medicine, University of Bern, and Agroscope, Bern, Switzerland; <sup>‡</sup>Institute of Animal Pathology, Vetsuisse-Faculty, University of Bern, Bern, Switzerland; and <sup>§</sup>Division of Clinical Radiology, Department of Clinical Veterinary Medicine, Vetsuisse-Faculty, University of Bern, Bern, Switzerland\*Corresponding author email: [nathalie.fouche@vetsuisse.unibe.ch](mailto:nathalie.fouche@vetsuisse.unibe.ch)**Keywords:** horse; incoordination; neoplasia; neurologic patient; tumour**Summary**

Neoplasia is a rare cause of ataxia in horses. This report describes a 2-year-old colt presented with sudden-onset ataxia in which a cervical vertebral osteosarcoma causing severe compression of the spinal cord was diagnosed. Radiological changes included a large osteolytic lesion in the vertebral body, the vertebral arch, the right cranial articular process and the right transverse process of C4, interrupting the borders of the vertebral foramen and the right transverse foramen. Myelography revealed a marked spinal cord compression. Necropsy confirmed the presence of a well-demarcated, invasive and firm mass protruding from the fourth cervical vertebral body that led to severe compression of the spinal cord. In spite of its strongly pleomorphic nature, the detection of osteoid confirmed the diagnosis of a central osteosarcoma of the combined type. To the best of our knowledge, a primary single vertebral osteosarcoma causing ataxia in a juvenile horse has not previously been reported, and findings of this case report could help in the diagnostic work-up of similar cases.

**Introduction**

Ataxia associated with spinal cord disease is common in horses (Furr *et al.* 2015). Major causes include equine herpesvirus 1 myeloencephalopathy (Donaldson *et al.* 1998; Friday *et al.* 2000; Olsen 2001) or cervical stenotic myelopathy (Hahn 2006), with the latter being a major cause of ataxia in young animals (Nout *et al.* 2003). Primary or metastatic neoplasia also causes ataxia in horses, albeit infrequently and various tumour types such as haemangiosarcoma (Newton-Clarke *et al.* 1994), lymphosarcoma (Shamis *et al.* 1984; Kannegieter *et al.* 1987; Zeman *et al.* 1989), angioma (Palmer *et al.* 1960), plasma cell myeloma (Drew and Greatorex, 1974), primary meningeal lymphoma (Lester *et al.* 1992), metastatic leiomyosarcoma (Kawabata *et al.* 2016), metastatic melanoma (Rodriguez *et al.* 1998; Patterson-Kane *et al.* 2001) and metastatic carcinoma (Joswig *et al.* 2013) have been reported to cause neurological disease and incoordination.

Osteosarcomas are rare tumours in equids, usually involving the osseous structures of the head (Bush *et al.* 2007; Springer *et al.* 2010; Leonardi *et al.* 2012; Leite *et al.* 2019) or the extremities (Zaruby *et al.* 1993; Nelson *et al.* 1998; Jenner *et al.* 2003; Bush *et al.* 2007; Cillan-Garcia *et al.* 2010; Gutierrez-Nibeyro *et al.* 2010; Kilcoyne *et al.* 2010; Koch *et al.*

2014). Risk factors associated with the development of osteosarcoma in horses are unknown due to the low number of reported cases. Factors such as hormonal influence as well as body size, height and weight and rapid bone growth, among others, seem to play a major role in the development of osteosarcoma in humans and dogs (Makielski *et al.* 2019), but whether the same factors play a role in the development of equine osteosarcoma remains unclear. According to the literature, all age groups can be affected by osteosarcomas (Bush *et al.* 2007) and foals as young as 7 weeks of age have previously been diagnosed with this condition (Livesey *et al.* 1986). Clinical signs associated with osteosarcomas in horses are not pathognomonic and largely depend on location and extent of the tumour growth (Zaruby *et al.* 1993; Nelson *et al.* 1998; Jenner *et al.* 2003; Bush *et al.* 2007; Cillan-Garcia *et al.* 2010; Jenner 2010; Kilcoyne *et al.* 2010; Leonardi *et al.* 2012; Koch *et al.* 2014; Leite *et al.* 2019).

Primary vertebral osteosarcomas have a low prevalence in humans (Sundaresan *et al.* 1988) and other species, and there are no reports about primary vertebral osteosarcomas in horses. In veterinary science, they have only been described in dogs (Luttgen *et al.* 1980; Moore *et al.* 2000; Brellou *et al.* 2004; Krimins *et al.* 2017), cats (Luttgen *et al.* 1980) and rabbits (Weiss *et al.* 2011). This study reports the case of a colt affected by a primary vertebral osteosarcoma causing sudden-onset ataxia and describes clinical, radiographic, computed tomography, gross and histopathological findings.

**Case history and clinical findings**

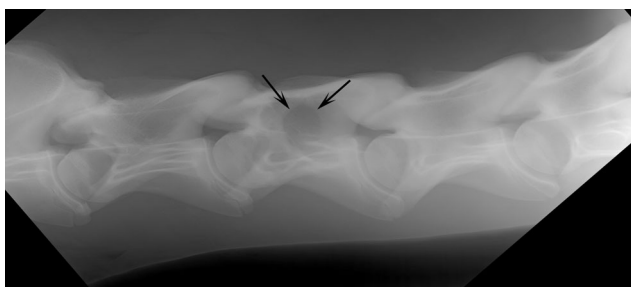
A 2-year-old Freiburger x PRE stallion was referred for evaluation of ataxia. The horse had been found in the field with suspected sudden onset of ataxia and was only minimally responsive to treatment with non-steroidal anti-inflammatory drugs. The private veterinarian had treated the horse with meloxicam (0.6 mg/kg bwt) and dexamethasone (0.04 mg/kg bwt) intravenously on the day of onset of clinical signs, and the owner had continued an oral treatment with meloxicam (0.6 mg/kg bwt) for another 3 days. After a total of 4 days of treatment at home, the horse was referred. Upon presentation to the referral hospital, the horse was in good general condition. Vital parameters were within normal limits. A CBC and serum biochemistry profile were unremarkable apart from a slight thrombocytosis ( $271 \times 10^9/L$ ; reference interval [RI], 104–244). The animal was bright and responsive

with normal mentation. There were no cranial nerve deficits, and the stallion was eating and drinking normally. Tail tone and anal reflex were normal, and the horse was defecating and urinating normally. There was no loss of skin sensation on the neck, the trunk or the front limbs. However, the range of the active neck movement was symmetrically reduced towards lateral, dorsal and ventral, whereas the passive movement could not be evaluated due to the horse's non-cooperative behaviour. Proprioceptive deficits were present in both front and hindlimbs. Those included a base-wide limb placement and swaying of the trunk during walking. During circling, the horse showed circumduction in the pelvic limbs and interference in the pelvic and thoracic limbs. Further neurological tests were not performed due to the horse's degree of uncoordination. The stallion displayed great difficulty coordinating his movements and showed a marked ataxia on all four limbs that was more pronounced in the hindlimbs. The proprioceptive deficits on both fore- and hindlimbs nearly made the horse fall at the walk (ataxia grade 4/5 according to Mayhew's grading system) (Mayhew *et al.* 1978). According to the clinical findings, a neuro-anatomical lesion was suspected in the cervical spinal cord.

### Diagnostic imaging

Left-to-right lateral radiographs (Vertex Vet X-ray system, Siemens, Germany; CR-IR 342, Fuji Photo Film, Japan, with FCR Fuji IP Cassette type CC 35.4 × 43 cm) of the cervical spine were performed standing under sedation. They showed a well-demarcated round geographic osteolysis involving the vertebral body and one side of the vertebral arch of the 4th cervical vertebra (C4) (Fig 1). An interruption in the outline of the floor of the vertebral foramen was observed at the mid-body of C4, and the dorsal border of this foramen was poorly defined. An aggressive mono-ostotic vertebral lesion was diagnosed.

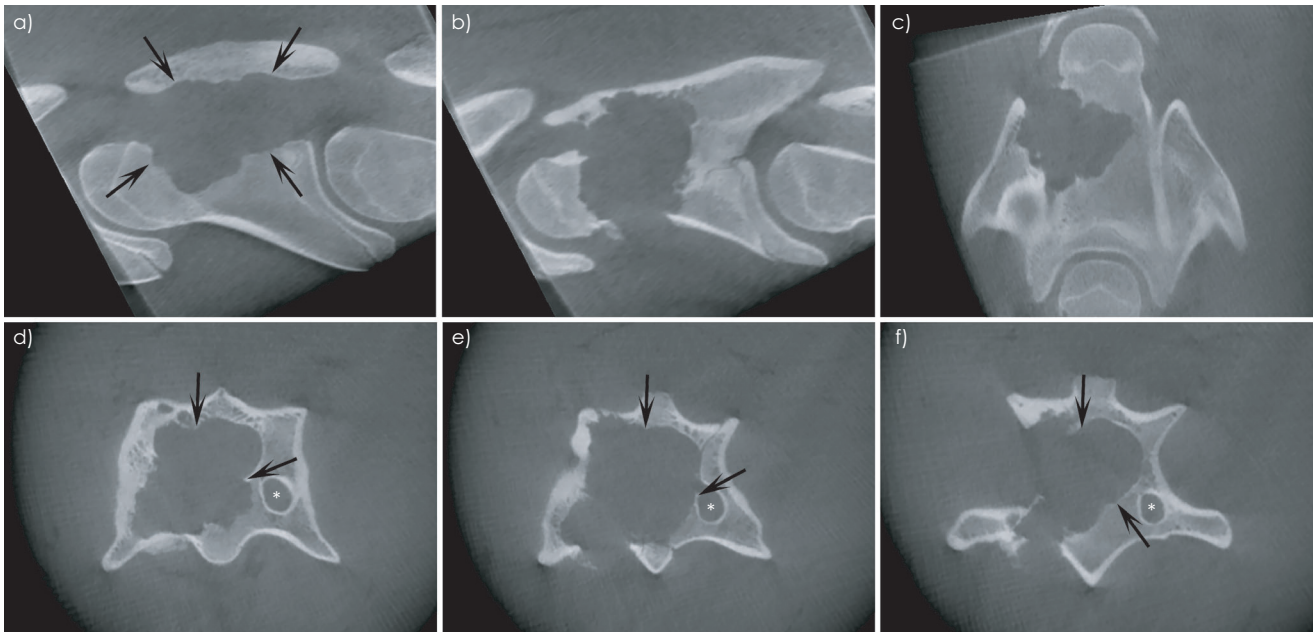
In order to further characterise the lesion and its relationship with the spinal cord and clinical signs, an examination using cone-beam computed tomography (CBCT; O-arm, Medtronic, Minneapolis, Minnesota, USA) under general anaesthesia was performed with data acquisition before and after myelography using the same parameters (120 kV, 32 mA, 240 mAs). The image data were reconstructed using a bone algorithm into a slice thickness of 0.833 mm and a pixel size 0.415 × 0.415 mm. The native scan included the caudal aspect of the 3rd cervical vertebra (C3)



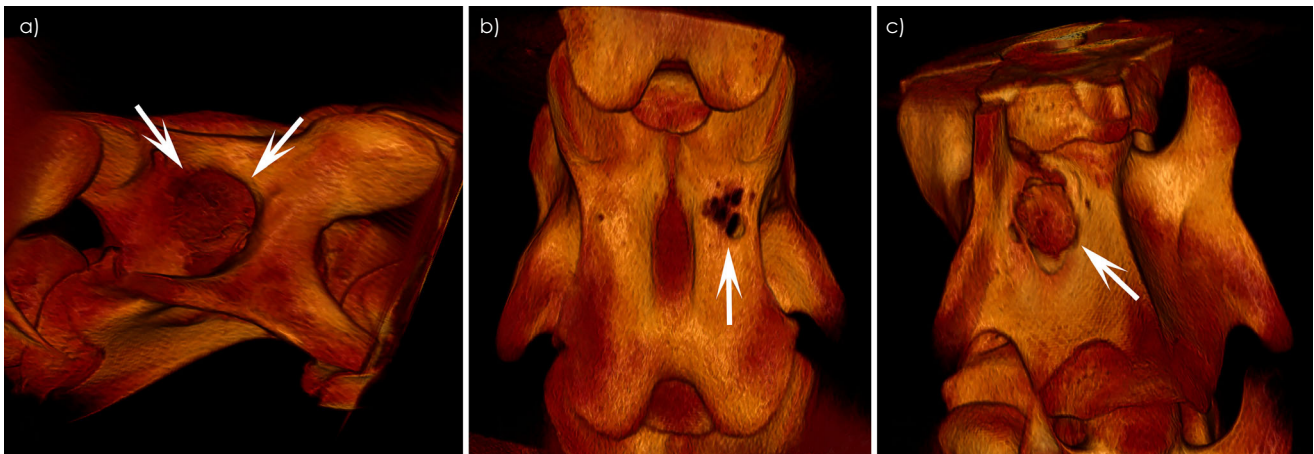
**Fig 1: Right-to-left lateral radiograph of the cervical spine, centred on C4. A sharply delineated, rounded osteolytic lesion is present in the mid-aspect of C4 involving one of the laminae (black arrows) and interrupting the floor of the vertebral canal.**

to the cranial aspect of the 5th cervical vertebra (C5). It showed a mildly expansile, large osteolytic lesion in the mid-part of C4 (Figs 2 and 3). This lytic process showed irregular borders and was centred on the right border of the vertebral foramen. It involved the vertebral body, the right aspect of the vertebral arch, the borders of the right transverse foramen, the right cranial articular process and the right transverse process. It reached from the cranial to the caudal vertebral physis and caused multifocal cortical interruptions on the right side of the dorsal arch, the lamina and the ventral aspect of the vertebral body. In some areas, the lysis was surrounded by a minimal amount of ill-defined sclerosis. There was a mild and mainly laminar periosteal reaction at the ventral aspect of the vertebral body, also interrupted by the lytic lesion. In its dorsal, cranial and caudal aspects, the vertebral foramen of C4 showed an undulating widening of its osseous boundary.

After the first set of native CBCT images, a cerebrospinal (CSF) tap was performed as previously described (Johnson and Constantinescu, 2000). In brief, the area caudal to the external occipital protuberance was clipped and aseptically prepared. The head was maintained in a flexed position, and a spinal needle (BD Spinal Needle, 20 GA 3.50 IN, Becton Dickinson, Madrid, Spain) was introduced in the midline of the neck, at the level of the cranial borders of the atlas wings. After penetration of the subarachnoid space, cerebrospinal fluid was drained. As the cerebrospinal fluid was draining very slowly, only 30 mL were withdrawn prior to the injection of the same amount of diluted non-ionic iodinated contrast medium (Iohexol; Accupaque™, GE Healthcare, Glattbrugg, CH; 300 mgI/mL, diluted with NaCl to 200 mgI/mL). The head was maintained in an elevated position for 5 min prior to imaging. On the CBCT myelography, the spinal cord was markedly flattened laterolaterally and displaced left dorsally along the entire length of C4, with the punctum maximum at the level of the previously described osseous lesion (Fig 4). The right and ventral contrast columns were interrupted, with an overall narrowing of the subarachnoid space at C4. This was caused by a large soft tissue attenuating lesion identified to the right of the vertebral canal, decreasing the diameter of the vertebral canal. This mass extended through the previously described osseous defects, causing additional compression and displacement of the cervical fat planes dorsolaterally. As CBCT did not allow a clear outline of the peripheral borders and visualisation of the internal structure of the mass, an ultrasonographic examination was performed (Logic E9, GE, Germany; curvilinear transducer C3-10, set at 6 MHz). A well-bordered, heterogeneous mass was observed on the right side of C4 and extending through an osseous defect into the vertebral canal (Fig 5). The mass was overall hypoechoic to the surrounding musculature and contained several, variably sized, ovoid, anechoic regions in both the peripheral and intravertebral parts. Additional pinpoint hyperechoic, mildly shadowing foci were observed in some regions. The hypoechoic part of the mass showed discrete, mainly peripheral vascularisation using colour and power Doppler. The conclusion after imaging was an osteolytic, mono-ostotic vertebral lesion causing extraradical compression on the spinal cord and showing invasion into the peripheral soft tissues. Considering the aggressive imaging characteristics, centred on the vertebral body and the mainly solid structure of the mass, a neoplastic process of vertebral origin was suspected.



**Fig 2:** Sagittal (a, b), dorsal (c) and transverse (d–f) multiplanar reconstructed cone-beam CT images (WL: 600; WW: 3000) showing the large osteolytic lesion in C4. Image (a) was made in the median plane of C4, (b) at the level of the right lamina and (c) at the ventral border of the transverse foramina. Transverse images d–f were made, respectively, at the cranial, mid- and caudal third of the lesion. Note the major disruption of the borders of the vertebral canal (black arrows) and the lack of visibility of the right transverse foramen. A nutrient foramen can be seen in image (e) connecting the left transverse foramen (black asterisk) and the vertebral canal. The left side of the images represents, respectively, the cranial (a, b) or the right side of the animal (c–f).



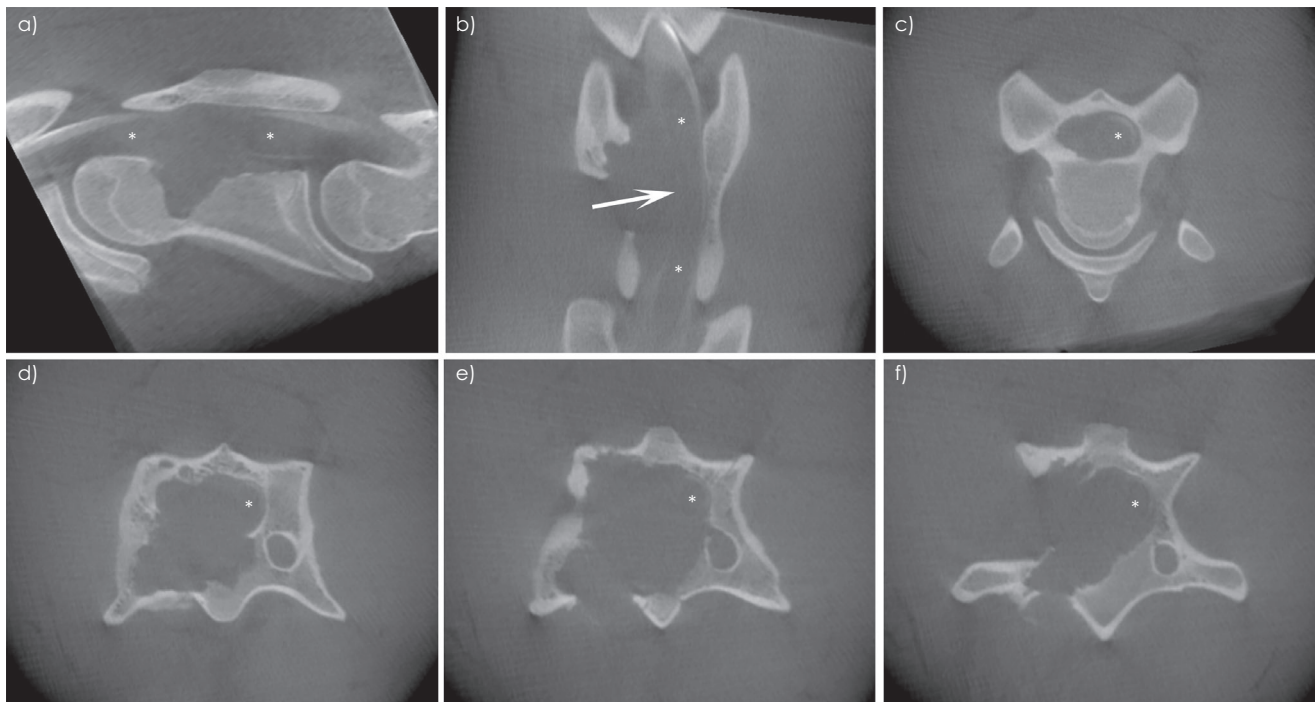
**Fig 3:** Volume rendered CT images of the cervical spine, showing the defects in C4 at the right lamina (a), right dorsal arch (b) and right ventral aspect of the vertebral body (white arrows). Cranial is, respectively, to the right (a) and top (b, c). The right side of the animal is, respectively, to the right (b) and left (c).

Cerebrospinal fluid analysis was performed and revealed an increase in protein (1.10 g/L; RI 0.28–0.77) as the only abnormality. Due to the poor prognosis, euthanasia was recommended.

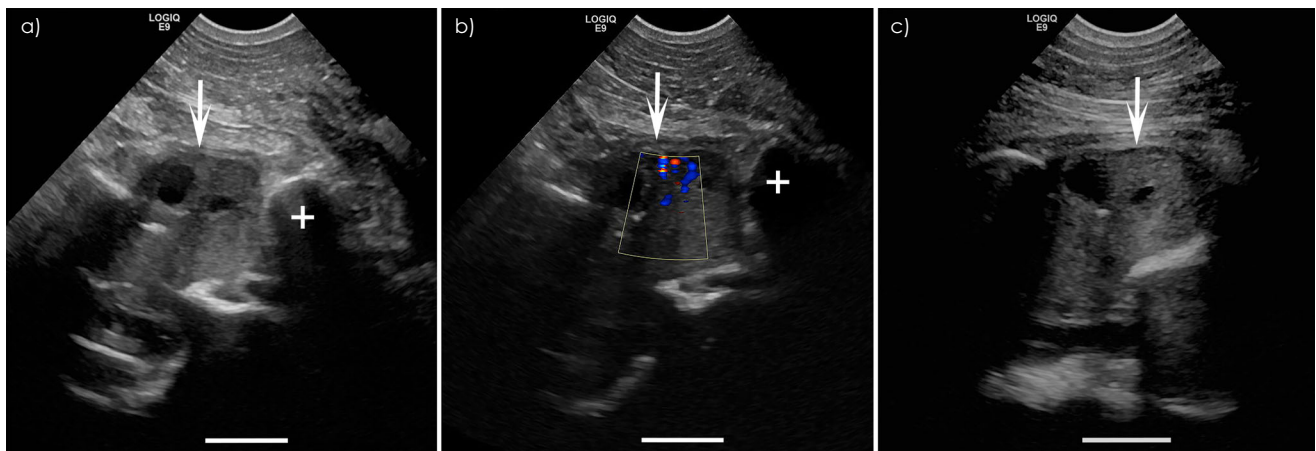
### Post-mortem findings

A full post-mortem examination was performed following euthanasia. The examination of the cervical region revealed the presence of a well-demarcated, yellow, invasively growing and firm mass, which measured approximately

9 × 6 × 5 cm and originated from the right ventrolateral aspect of C4. The mass grew into the vertebral canal with consequent diameter decrease and was associated not only with severe compression of the spinal cord on a length of approximately 5 cm (Fig 6), but also with severe osteolysis, which led to focal cavity formation between the ventral crest and the right transversal process (Fig 6). Also, there were occasional greenish to greyish areas visible whose shape was compatible with the anechoic lesions observed in the ultrasound (Fig 6). Apart from a focal brown discoloration of the dorsal sclera of the right eye and multifocal, small chronic



**Fig 4:** Sagittal (a), dorsal (b) and transverse (c–f) multiplanar reconstructed cone-beam CT images (WL: 600; WW: 3000) after myelography. Images a, d–f are made at the same level as in Fig 2; b is located at the level of the vertebral canal and image c at the cranial aspect of C4. There is marked thinning of all subarachnoid contrast columns over the entire length of C4, showing a complete interruption right ventrally at the level of the lysis. Marked extradural compression and left dorsal displacement of the spinal cord is noted (white arrows). The location of the spinal cord is indicated by the white asterisks. As mentioned in Fig 2, a nutrient foramen is seen in image (e) connecting the left transverse foramen and the vertebral canal. The left side of the images represents, respectively, the cranial (a) or the right side (b–f) of the animal.



**Fig 5:** Transverse (a, b) and longitudinal (c) ultrasonographic images showing a well-defined heterogeneous hypoechoic mass (white arrows), extending from the vertebral canal laterally through a defect in the right vertebral lamina. Mild vascularisation was observed at the periphery of the mass using colour Doppler interrogation (b). The right transverse process is indicated by the white + for orientation. For all images, the transducer was positioned on the right side of the neck at the level of C4. The left side of the images represents, respectively, the dorsal (a, b) or cranial aspect of the animal. The white bar at the bottom of every image represents a 2 cm reference.

ulcerations of the gastric mucosa, no further lesions were identified upon gross necropsy. Tissue samples from the mass, the cervical spinal cord and the right eye were immediately collected and fixed in 10% neutral buffered formalin for 24 h, embedded in paraffin, cut at 4  $\mu$ m and stained with

haematoxylin and eosin (H&E) for further histological evaluation. Several cross-sections of the cervical mass were assessed and revealed a non-encapsulated, moderately well-demarcated, moderately to highly cellular and infiltrative growing neoplasia. This neoplasia was composed of

mesenchymal cells that grew in streams, strands, bundles and occasionally in small whorls, which were embedded in variable amounts of fibrovascular, lax to compact stroma. Occasionally, small clusters of amorphous, eosinophilic material (compatible with osteoid) surrounded the neoplastic cells (**Fig 6**). These were polygonal to fusiform, measured between  $7 \times 20$  and  $12 \times 50 \mu\text{m}$ , had moderately distinct cell borders, a small amount of inhomogeneous, eosinophilic cytoplasm and a central, irregularly shaped nucleus with coarse chromatin and an indistinct nucleolus. Anisocytosis and anisokaryosis were severe, and mitotic figures were only rarely observed in ten  $400\times$  high-power-fields. Binucleated neoplastic cells or cells displaying large nuclei measuring up to  $15 \mu\text{m}$  in diameter were also occasionally observed. Moderate numbers of lymphocytes infiltrated multifocally the neoplasia, and there were occasional acute haemorrhages visible. No necrosis was clearly visible in four tissue slides from the mass. In addition, the muscle fibres of the skeletal muscle surrounding the neoplasm displayed a severe atrophy. In spite of the diversity of growth patterns displayed by the neoplastic cells, the observation of osteoid surrounding the cells justified a final diagnosis of a central osteosarcoma of the combined type for this neoplasia. Cross-sections from the spinal cord at the level of C4 and C5 revealed a severe midline shift towards left, with multifocal, severe Wallerian degeneration. This was characterised by axonal swelling (spheroid formation), distention of the myelin sheaths and replacement of damaged fibres by macrophages containing intracytoplasmic myelin debris (**Fig 6**), with multifocal activation of the endothelial cells of the small- and medium-sized vessels. The dorsal scleral lesions in the right eye corresponded to a mild lymphocytic episcleritis and were considered a secondary unrelated finding.

## Discussion

This report describes the findings in a 2-year-old horse diagnosed with a primary vertebral osteosarcoma. It is the first report to describe ataxia as a clinical sign of an osteosarcoma in a horse.

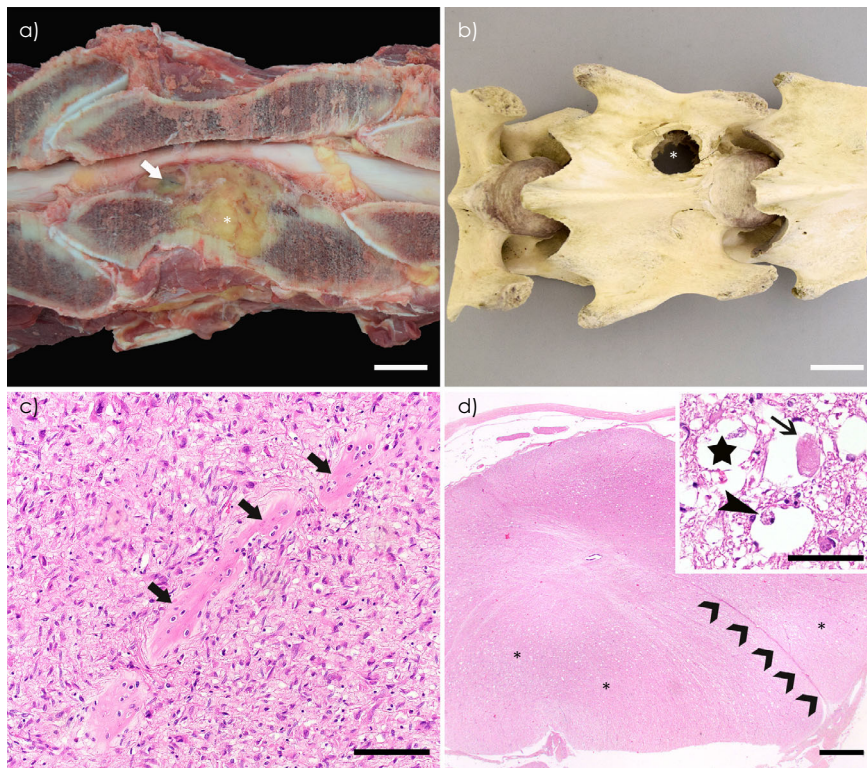
Laboratory analyses of the blood and the CSF tap showed only mild and unspecific changes. The horse had a mild thrombocytosis as the only abnormality in a CBC and serum biochemistry profile, which was interpreted as a non-specific sign of cancer-related inflammation. Thrombocytosis as a paraneoplastic sign has been identified with human renal cell carcinoma and is associated with poor survival (Cho *et al.* 2011; Hutterer *et al.* 2015), potentially reflecting tumour aggressiveness (Bensalah *et al.* 2006). A haematological finding that has repeatedly been described in horses with osteosarcoma is a normochromic, normocytic anaemia (Koch *et al.* 2014; Leite *et al.* 2019), but this patient had no anaemia. Cerebrospinal fluid analysis is often unchanged in equids with neoplasia affecting the nervous system (Zeman *et al.* 1989; Rodríguez *et al.* 1998; Southwood *et al.* 2000; Hirsch *et al.* 2009). The increase in total protein of the CSF tap is a non-specific abnormality and has formerly been reported in horses with lymphoma of the central nervous system (Adolf *et al.* 2001).

Diagnostic imaging was essential in the diagnostic work-up of the case, and findings were similar to those previously described. Vertebral osteosarcomas are described as osteolytic lesions in the vertebral body (Peyrade *et al.* 1995)

on radiography and computed tomography (Moore *et al.* 2000; Yalniz *et al.* 2009). The description of a heterogeneous mass displaying a mixed osteosclerotic–osteolytic appearance from the human literature (Orguc *et al.* 2014) is also in accordance with the diagnostic imaging findings of our patient. Extradural compression of the spinal cord due to a neoplastic mass or a pathological fracture can cause ataxia. However, the latter was considered unlikely in our case due to the lack of compatible radiographic signs, and the osteolysis of the borders of the vertebral foramen rather suggested the presence of a neoplastic mass. This suspicion was confirmed on the CT-myelography, which revealed the presence of a large extradural mass that compressed the spinal cord, thus explaining the spinal ataxia described in the anamnesis. Notably, no lesions compatible with fractures were observed in any of these examinations. In order to further characterise the soft tissue lesions, an ultrasound examination was performed, revealing a heterogeneous mass extending into the osseous defect. The hyperechoic foci potentially represent multifocal calcifications as previously described in a horse with an appendicular osteosarcoma (Gutiérrez-Nibeyro *et al.* 2010). The occasional anechoic regions were most likely due to focal tumour necrosis, even if this suspicion could not be confirmed in the histopathological analysis of four tissue slides from the mass.

Reports about potential treatment options for horses with osteosarcomas are limited to the head and the extremities (Gutiérrez-Nibeyro *et al.* 2010; Springer *et al.* 2010). One report describes the surgical removal of an osteosarcoma of the fourth tarsal and the third and fourth metatarsal bone followed by a treatment with absorbable beads containing cisplatin (Gutiérrez-Nibeyro *et al.* 2010). Surgical removal and radiation therapy were also successful in the treatment of an osteoblastic osteosarcoma in the nasal passage of a 27-year-old Thoroughbred gelding (Springer *et al.* 2010). Nevertheless, most horses diagnosed with an osteosarcoma are subjected to euthanasia due to the locally invasive and destructive nature of the tumour, independent of the tumour localisation (Bush *et al.* 2007; Joswig *et al.* 2013; Leite *et al.* 2019). Primary vertebral osteosarcomas occurring in humans carry a poorer prognosis than the appendicular forms due to the difficulties of the surgical treatment (Lefebvre *et al.* 2013). The advanced stage of the disease and the tumour localisation in the vertebral spine meant that there was no option beside euthanasia in the horse presented in this report.

The final diagnosis of a primary vertebral osteosarcoma of the combined type was based on the pathological and histopathological examination of the tumour. Osteosarcomas have formerly been described as firm, expansive and often invasive mineralised masses that distorted the normal tissue architecture with pronounced adjacent periosteal bone formation and central areas of necrosis (Bush *et al.* 2007). While calcification was not prominent, the other tumour characteristics were consistent with the findings in this patient. Metastatic lesions to other organs can occur in equids with osteosarcomas (Livesey *et al.* 1986; Kilcoyne *et al.* 2010), but it is not uncommon to find a single primary tumour (Zaruby *et al.* 1993; Bush *et al.* 2007; Cillan-García *et al.* 2010; Leonardi *et al.* 2012) as described in this report. The true metastatic behaviour of equine osteosarcomas is unclear due to the low number of reported cases (Jenner 2010). The final diagnosis of an osteosarcoma was based on the demonstration of osteoid directly formed by the malignant



**Fig 6:** Macroscopical and histological analysis of the cervical compressive osteosarcoma and overlying cervical spinal cord (a) Dorsal view of the mass (asterisk) following removal of the vertebral arches between C3 and C5. The mass grew from the vertebral body and protruded into the vertebral canal, with severe, focal-extensive compression of the spinal cord. A greenish to greyish, ovoid area is visible in the caudal aspect of the mass (large arrow). Bar 2 cm. (b) Ventral aspect of the body from the fourth cervical vertebra following boiling. Severe osteolysis led to a cavity formation (asterisk) between the ventral crest and the right transversal process. Bar 2 cm. (c) Histopathological analysis of the cervical mass. The neoplastic cells were occasionally embedded in amorphous, eosinophilic material, which was compatible with osteoid (large arrow). H&E, bar, 100  $\mu\text{m}$ . (d) Histopathological analysis of the overlying cervical spinal cord. A severe midline shift with distortion of the ventral median fissure (large arrowheads) with severe, widespread Wallerian degeneration (asterisks) could be observed. H&E, bar, 1 mm. (Inset) Larger magnification of the affected cervical white matter displaying several typical features of Wallerian degeneration, namely spheroid formation (thin arrow), distention of the myelin sheaths (star) and replacement of damaged fibres by macrophages containing intracytoplasmic myelin debris (thin arrowhead). H&E, bar, 50  $\mu\text{m}$ .

cells in histopathology (Jo *et al.* 2014), as previously described in other case reports (Jenner *et al.* 2003; Bush *et al.* 2007; Cillan-Garcia *et al.* 2010; Gutierrez-Nibeyro *et al.* 2010; Koch *et al.* 2014; Leite *et al.* 2019).

This case report adds a differential diagnosis to the list of uncommon causes of spinal ataxia in young horses. Radiographic and CT myelographic images and findings as well as pathological and histopathological descriptions presented in this report can aid in the diagnosis of a similar clinical case.

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## Authors' declaration of interests

No conflicts of interest have been declared.

## Ethical animal research

Consent was gained from the owner for all diagnostic procedures and the use of case material for teaching and research purposes.

## Authorship

N. Fouché, I. Berenguer Veiga and E. Van der Vekens contributed to study design, study execution, data analysis and interpretation and preparation of the manuscript. S. Oesch, L. Küchler, L. Unger and M. Molazem contributed to study design, study execution, and data analysis and interpretation. All authors gave their final approval of the manuscript.

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