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NOTE

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Blindness associated with nasal/paranasal lymphoma in a stallion

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ABSTRACT. A 29-year-old stallion presented with bilateral blindness following the chronic purulent nasal drainage. The mass occupied the right caudal nasal cavity and right paranasal sinuses including maxillary, palatine and sphenoidal sinuses, and the right-side turbinal and paranasal septal bones, and cribriform plate of ethmoid bone were destructively replaced by the mass growth. The right optic nerve was invaded and involved by the mass, and the left optic nerve and optic chiasm were compressed by the mass which was extended and invaded the skull base. Histologically, the optic nerves and optic chiasm were degenerated, and the mass was diagnosed as lymphoma which was morphologically and immunohistochemically classified as a diffuse large B-cell lymphoma. Based on these findings, the cause of the blindness in the stallion was concluded to be due to the degeneration of the optic nerves and chiasm associated with lymphoma occurring in the nasal and paranasal cavities. To the best of our knowledge, this is the first report of the equine blindness with optic nerve degeneration accompanied by lymphoma.

KEY WORDS: blindness, horse, lymphoma, nasal and paranasal cavities

Blindness associated with damage to the optic pathway is not uncommon in horses. The striking feature of the damage is degeneration and/or atrophy, and there are a variety of possible causes, including trauma, inflammation and glaucoma [2–4, 13]. Tumors involving the optic pathway can also be a cause of blindness. Horses with tumor in the nasal and paranasal cavities develop various non-specific clinical signs, and the blindness can occur in relation to tumor growth and invasion [5, 7, 8, 16]. Although the nasal and paranasal tumors in horses are relatively uncommon [5, 8], the occurrence of various types of epithelial and mesenchymal tumors has been recorded. The common types of tumor in the nasal and paranasal cavities have been presented as squamous cell carcinoma, adenocarcinoma, bone and dental tumors, fibrosarcoma and hemangiosarcoma [8]. Previously, squamous cell carcinoma, adenocarcinoma and undifferentiated tumor had been identified as a cause of blindness by nasal and paranasal tumors of horses [5, 8, 16].

Lymphoma is a malignant neoplastic disease originating from lymphoid tissue outside of the bone marrow. In horses, lymphoma can occur at any age, and it is one of the most common malignant neoplastic disease [1, 18]. The incidence is rare, but nasal and paranasal cavities have also been included as the occurrence site of lymphoma [5, 8]. The major clinical manifestations of equine lymphoma vary depending on the location and the degree of organ involvement [1], and lymphoma with central nervous system and peripheral nerve involvements have developed neurological signs [9, 11, 15, 17, 19, 20]. However, blindness accompanied by lymphoma has not been reported in horses.

In this paper, we present the first report of bilateral blindness caused by lymphoma in a stallion, which was considered to be primarily arising from the nasal/paranasal cavity.

A 29-year-old, Anglo-Arabian stallion, presented acute-onset of purulent discharge from right nasal cavity. The radiographic examinations demonstrated increasing opacity with the presence of free horizontal air-fluid interface in the right maxillary sinus area, and the stallion was clinically diagnosed as empyema. Advanced treatment was recommended, but the owner chose conservative treatment considering his age. The treatment was continued approximately for a month. Even though the stallion was treated with antibiotics for the following two months, improvement was transient and intermittent purulent drainage from the right nasal cavity was observed. The lesion of the right paranasal cavity was re-evaluated by radiographic examination and revealed that the area of the opacity had been expanded in the area of the right maxillary and ethmoidal sinuses. Subsequently, the stallion presented with right cheek swelling with self-destruction. The exophthalmos and visual impairment of the right eye were also noticed. After about a month, bilateral visual impairment was suspected by observations, when the horse bumped a wall or

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door when pulling, and also stumbled on an obstacle. The neuro-ophthalmic examination resulted in bilateral absence of direct and indirect pupillary light reflexes, dazzle reflex and menace response, and the stallion was considered to have bilateral blindness. The stallion was euthanized due to its progressive condition, and the owner elected to use euthanasia. The whole body of the horse was submitted for the necropsy.

At necropsy, the stallion weighed 420 kg. In the dorsal view of the skull base, the invaded lesion from the sphenoid saddle nub into intracranial was observed. The right optic nerve was involved in the proliferated lesion until near the optic chiasm, and the tissue boundary of the right optic nerve was not confirmed. The lesion was formed adjacently and compressively to the left optic nerve and pituitary gland (Fig. 1). The skull sagittal section revealed the presence of a mass, composed of heterogeneous proliferation of yellow to whitish tissue with hemorrhagic and necrotic areas, occupying the right caudal nasal cavity and right paranasal sinus including maxillary, ethmoidal, palatine and sphenoid sinuses (Fig. 2). The right-side turbinal and paranasal septal bones, and cribriform plate of ethmoid bone were then destructively replaced by the mass growth. The skull cross-section revealed the invasion of the mass into the right orbit with destruction of inferonasal and nasal areas. And, the section also revealed the invasion of the mass into the left palatine and sphenoidal sinuses, and the presence of the left optic canal and optic nerve. No relevance of the mass to soft palate, pharynx, larynx and tonsil was observed grossly, and no abnormalities were observed in each of the organs. The right maxillary and pharyngeal lymph nodes were slightly enlarged.

The collected tissues during the necropsy were fixed in 10% neutral-buffered formalin, embedded in paraffin wax and cut into 4-μm-thick sections. The sections were stained with hematoxylin and eosin, and subjected to light microscopic examinations. Histologically, the mass, which occupied the right caudal nasal cavity and right paranasal sinus, was composed of diffuse proliferation of neoplastic lymphoid cells. The proliferations were supported by thin and loose fibrous and fibrovascular stromas. The neoplastic lymphoid cells had single, large, round to oval but often cleaved nuclei with single or multiple nucleoli, and variable amounts of eosinophilic cytoplasm (Fig. 3). The nuclei of neoplastic cells were approximately 2 to 3 times the size of red blood cell diameter (Fig. 3 inset). The mitotic figures were frequently observed, and the average number in 10 fields using 400-high power magnification was 11.3. Among the neoplastic large lymphoid cells, smaller scattered lymphocytes had single and round finely chromatic nuclei with a single nucleolus. Lymphoid hyperplasia was an evident cause of the enlargement which were grossly observed in right maxillary and pharyngeal lymph nodes. In the right optic nerve in the vicinity of the optic chiasm, the infiltration of the neoplastic lymphoid cells into the nerve bundles and nerve septum was observed. A wide range of nerve bundles was severely degenerated. The optic nerves were vacuolated and demyelinated, and spheroids were sporadically formed (Fig. 4). Obesity glial cells were found among the nerve bundles, and foamy macrophages infiltrated the degenerated nerve bundles or nerves. Similar degenerated lesions of nerves were observed in the optic nerve of the right orbit, but the lesion was confined to only several bundles. In the optic chiasm, degeneration of the right optic nerve bundles was continuously observed, and the left optic nerves were similarly severely degenerated. Degenerative lesions of the optic nerves were observed focally in the optic nerve bundles of the left orbit. In bilateral eyes, ocular tracts, visual pathways and visual cortices, histological abnormalities to contribute to a cause of the blindness were not observed.

Immunohistochemical examination was performed by the avidin-biotin-peroxidase complex procedure (Vectastain Elite ABC Kit; Vector Laboratories, Burlingame, CA, U.S.A.) to identify the type of neoplastic lymphoid cells. The primary antibodies used were mouse monoclonal antibody against human CD79α (clone HM57; Dako, Glostrup, Denmark) and rabbit polyclonal antibodies against CD20 (Thermo Fisher, Scientific Inc., Waltham, MA, U.S.A.) and CD3 (Dako). Most of the large neoplastic lymphoid cells were positively stained for CD79α (Fig. 5) and CD20, but negative for CD3. The smaller lymphoid cells distributed among the neoplastic cells were stained for CD3 (Fig. 6).

Based on the gross and histological findings, the blindness in the stallion was concluded to be due to the degeneration of the optic nerves and chiasm. The invasion and growth of the tumor that occurred in nasal and paranasal cavities were regarded as the cause of the degeneration. The tumor was composed of the neoplastic lymphoid cells, and it was diagnosed as lymphoma.

The various causes of equine blindness associating with degeneration of optic pathway have been reported [2–4, 13]. It is relatively uncommon, but the nasal and paranasal sinus tumors have a potential to provoke the visual impairment caused by damage of the optic pathway in relation to their growth and/or invasion. Previously, the three different types of tumors, i.e., squamous cell carcinoma, adenocarcinoma and undifferentiated tumor, in nasal and paranasal cavities have been identified as a cause of blindness in horses [7, 8, 16]. In one of these cases, an 8-year-old Quarter Horse mare presented with acute blindness, which was clinically diagnosed as central origin blindness and active retinitis. An obstruction by squamous cell carcinoma was found in the nasal passage, and the cause of the blindness in the mare was detected as pressure by the expanding tumor deforming the ethmoid and sphenoid bones resulting in compression of the optic tracts [7]. In the case of adenocarcinoma, the complete bilateral devascularization of the retinas was clinically diagnosed in an 8-year-old thoroughbred mare. The cause of the blindness was confirmed as the tumor, which occupied the olfactory and frontal areas of the left hemisphere of the brain and part of the left frontal sinus [16]. Finally, a 10-year-old thoroughbred castrated cross horse presented with blindness with pale optic disc and retinal vasculature atrophy. The pathogenesis of the blindness in the horse was due to growth of an undifferentiated tumor in the sphenoid palatine sinus causing damage to the optic nerve [8]. In the present case of a 29-year-old Anglo-Arabian stallion, the right side of the visual impairment had been clinically noted prior to the bilateral blindness, and severe replacement of the lymphoma involving the optic nerve was found in the right caudal nasal and paranasal cavities. From these findings, the visual impairment of the right site was considered to have first occurred by direct invasion damage from the lymphoma occurring in the right nasal and paranasal regions. On the other hand, infiltration of lymphoma to the left optic nerve was not found, but the optic nerve had degenerated, and lymphoma in close contact with the growth of the left optic nerve and chiasm was observed. The visual

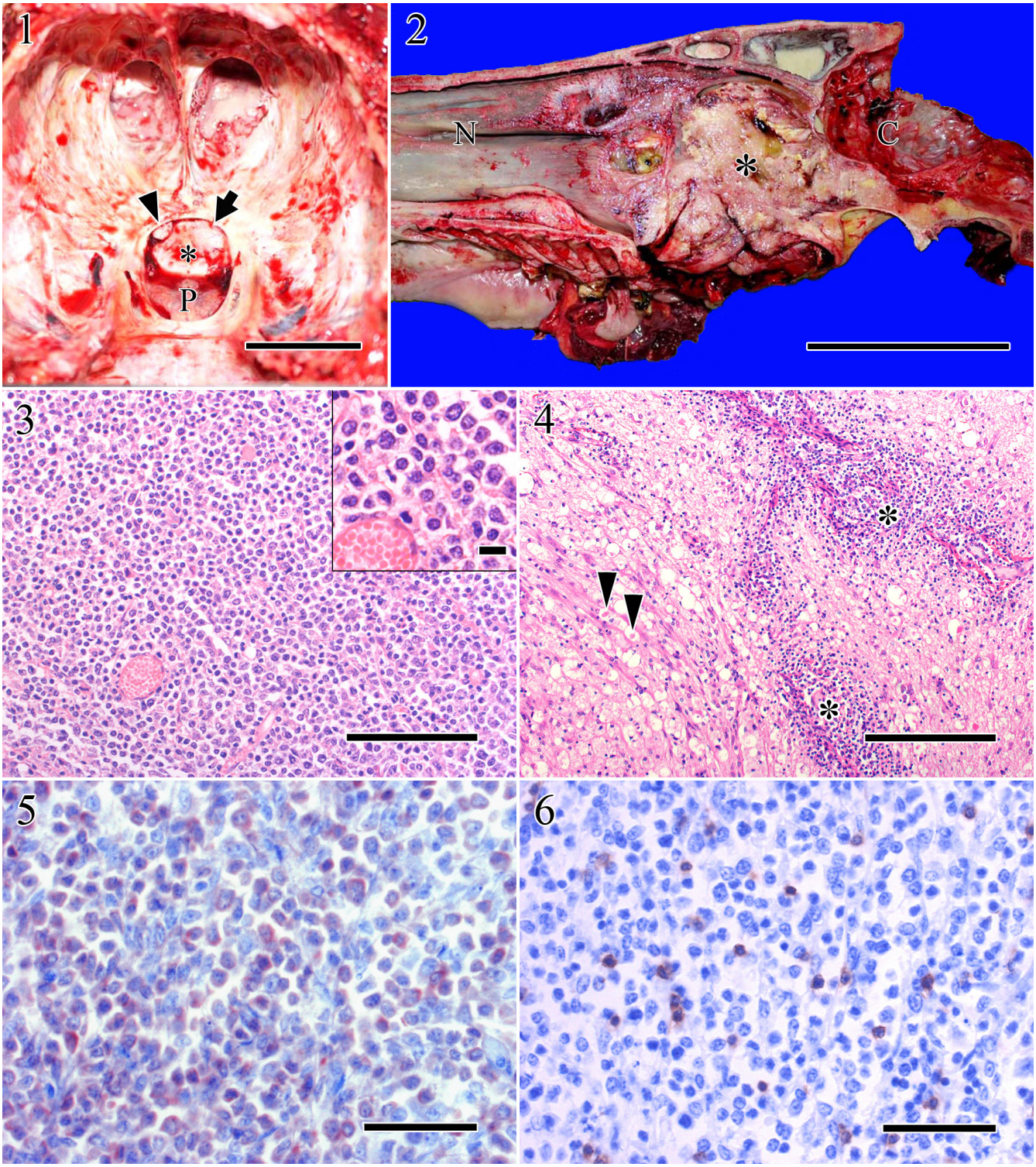

Fig. 1. Gross photograph of the dorsal view of the stallion's skull base. The proliferated lesion (∗) invaded the intracranium with involvement of the right optic nerve (arrow). The lesion also locates adjacently and compressively to the left optic nerve (arrowhead) and pituitary gland (P). Bar=3 cm.

Fig. 2. Gross photograph of the sagittal section of the stallion's right skull. The mass (∗) has occupied the caudal nasal and paranasal regions. N: nasal cavity. C: cranial cavity. Bar=15 cm.

Fig. 3. The mass in the right caudal nasal and paranasal regions is composed of a diffuse proliferation of neoplastic lymphoid cells. HE. Bar=200 μm. (inset) Higher magnification of Fig. 3. The neoplastic lymphoid cells have a large nucleus 2 to 3 times the diameter of red blood cells. HE. Bar=30 μm

Fig. 4. Histological photograph of right optic nerve in the vicinity of the optic chiasm. Neoplastic lymphoid cells infiltrate the nerve septum and the surrounding nerves (∗). A wide range of nerves is degenerated, and vacuolation of the nerves and spheroids (arrowheads) is formed. HE. Bar=500 μm.

Fig. 5. Most of the proliferated large neoplastic lymphoid cells are positively stained for CD79α. Immunohistochemistry for human CD79α counterstained with hematoxylin. Bar=50 μm.

Fig. 6. Scattered smaller lymphocytes are positively stained for CD3. Immunohistochemistry for CD3 counterstained with hematoxylin. Bar=50 μm.

impairment of the left side was considered to have occurred secondarily as a result of the disturbance compression of optic nerve and/or optic chiasm by lymphoma, which invaded the skull base. There has not been any report of equine blindness associating with nasal and paranasal lymphomas, to the best of our knowledge; this is the first report of the blindness in horses with optic pathway involvement by lymphoma occurring in nasal and paranasal cavities. The tumors including lymphoma that occur in the nasal and paranasal cavities of horses also develop other various non-specific clinical signs [5, 8]. The unilateral purulent nasal drainage and facial swelling, which was clinically noticed in the present case, are the most commonly seen in horses with nasal and paranasal tumors [5].

In the present case, although the lymphoma destructively invaded and distributed in the caudal nasal and paranasal cavities, no involvement of other lymphoid tissues was detected. The finding of the lesional distribution supported the lymphoma as a primary lesion originating from the nasal and/or paranasal region. The metastasis from the bone marrow could not be ruled out, but it was considered to be much less likely. The lymphoma in the present case may have arisen from lymphoid tissue, i.e. mucosal-associated lymphoid tissue or lymphocyte aggregates, which spread in the lamina propria mucosae of the normal upper respiratory systems of horses [12].

Morphological and immunohistochemical classification of equine lymphoma has previously been studied [6, 10, 14]. Morphologically, equine lymphoma can be classified into three different types, i.e. small-, large- and mixed-cell types. The small or large types can be determined according to their nuclear size against the diameter of erythrocytes, with 60% or more types of neoplastic cell belonging. Mixed-cell type consists both of small and large neoplastic lymphoid cells of the same immunophenotype. Immunohistochemistry using B- and/or T-cell markers can differentiate a type of neoplastic cell with consideration for the atypia of the expressed cells. It is also necessary to consider the ratio of cells expressing each antibody for the classification. The lymphoma in the present case was morphologically composed of diffuse large neoplastic lymphoid cell proliferation and small non-neoplastic lymphocyte infiltration. Immunohistochemically, the large neoplastic lymphoid cells expressed both B-cell markers of CD79α and CD20, but the small lymphocytes did not express the markers and smaller lymphocytes positively immunoreactive for a T-cell marker of CD3. Moreover, the number of T-cell infiltrations was not high, and the number of mitoses was high. According to the morphological and immunohistochemical findings, the lymphoma of the present case corresponded to the diffuse large B-cell lymphoma.

The major clinical manifestations of equine lymphoma vary depending on the location and degree of organ involvement [1]. The most common clinical signs are lymphadenopathy, lethargy, weight loss, edema and pyrexia [1]. Neurological signs, such as ataxia, paralysis and lameness, have been described as the result of lymphoma with central nervous system and peripheral nerve involvements [9, 11, 15, 17, 19, 20]. The present case showed that blindness in horses could be the result of lymphoma with optic pathway involvement. Although the occurrence of equine lymphoma in nasal and paranasal cavities is rare, it should be included in a differential diagnosis when a horse presents with clinical signs of blindness.

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