Spinal Oligodendroglioma with Diffuse Arachnoidal Dissemination in a Japanese Black Heifer

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ABSTRACT. A gelatinous focus with cystic spaces, was found in the posterior funiculus of the 2nd to 3rd lumbar levels of the spinal cord of a Japanese Black heifer, 2 years old, with clinical signs of severe dysstasia. Histopathological examination revealed that the spinal lesion consisted of multifocal and diffuse proliferation of round cells with abundant vacuolar cytoplasm and hyperchromatic nuclei. In the lesions there was a number of cystic spaces containing aggregates of small round cells. The neoplastic foci showed a honeycomb structure divided by thin blood vessels, representing typical lesions of oligodendroglioma. Diffuse and multifocal proliferation of these round cells were also recognized in the subarachnoidal space in the sacral spinal cord. Immunohistochemically, the proliferating round cells were negative for glial fibrillary acidic protein. Based on these morphological features, the case was diagnosed as lumbar spinal oligodendroglioma with diffuse arachnoidal dissemination.—KEY WORDS: bovine, oligodendroglioma, spinal cord.

Oligodendroglioma is a common brain tumor of animals, especially dogs [13], but only one bovine case has been reported [1]. Although both animal and human oligodendrogliomas are known to occur predominantly in the white matter of the cerebral hemispheres [9, 12, 13], spinal oligodendrogliomas are also recognized occasionally in children, and their clinical and pathological natures have been well demonstrated in several human cases [2]. In contrast, spinal cord tumors including oligodendrogliomas [5, 15] are rare in animals, except for extra-medullar tumors such as spinal nephroblastomas in young dogs [13], and bovine spinal gliomas are considered to be extremely unusual [1].

The present paper describes the morphological and immunohistochemical features of a spinal oligodendroglioma in a 2-year-old Japanese Black heifer and discusses the similarity between human and bovine cases.

A 2-year-old Japanese Black heifer suddenly developed hind limbs paralysis and dysstasia. The animal was treated by clysis with Ringer’s solution, but the clinical signs did not improve. The animal was euthanatized by electric shock 7 days after clinical onset at the owner’s request, and necropsied immediately. In the brain, there were no significant lesions, but congestion and yellowish discoloration was recognized in the posterior area of the 2nd to 3rd levels of the lumbar spinal cord. The cut surface in this area revealed a pale gelatinous focus, approximately 1 cm in diameter, with multiple cystic spaces filled with clear fluid, located mainly in the posterior funiculus (Fig. 1). The gelatinous focus was attached to the dura mater, and the subarachnoidal space was replaced by the gelatinous material. In the subarachnoidal space of the lower lumbo-sacral spinal cord, a small amount of fibrinous material, pale to tan in color, was distributed diffusely and widely.

Tissue samples were fixed in 10% formalin and routinely processed. Paraffin sections were stained with hematoxylin and eosin (HE), and some selected sections of the spinal cord were also stained with Luxol fast blue (LFB), Masson’s trichrome, Watanabe’s silver impregnation, and alcin blue (pH 2.5). Histopathological examination revealed that the lumbar spinal lesion consisted of multifocal and diffuse proliferation of neoplastic cells with cystic spaces (Fig. 2). The tumor mass was located mainly in the white matter, and the posterior funiculus were almost totally replaced by the proliferating tumor cells and cystic places. The neoplastic foci showed a honeycomb structure with solid proliferation of round cells, representing the typical appearance of oligodendroglioma (Fig. 3). Most neoplastic cells were round in shape with abundant clear cytoplasm and hyperchromatic central nuclei. The presence of cytoplasmic processes was not confirmed. In the tumor there were a number of blood vessels with thin vascular walls, while the endothelial cells did not show apparent hyperplastic or proliferative changes. There were also a few of well differentiated astrocytes with well defined eosinophilic cytoplasmic processes in the neoplastic foci. In contrast, at the periphery of the neoplastic foci, diffuse proliferation of these astrocytes was prominent. Within the cystic spaces, there were aggregates of small number of small round cells mimicking lymphocytes, with small hyperchromatic round nuclei and scanty cytoplasm. Mitoses of the neoplastic cells were extremely rare. The neoplastic cells invaded the leptomeninges, and the subarachnoidal space was filled by a proliferation of these cells. Diffuse and multifocal proliferation of the round cells and lymphocyte-like small round cells, were also seen in the subarachnoidal space in the 2nd and 3rd levels of the sacral spinal cord (Fig. 4). In this area, some foci consisted of aggregates of neoplastic cells, and some areas showed an organoid structure made up of tumor cells, a few astrocytes and their cytoplasmic processes (Fig. 5). Besides the spinal cord there was no evidences for metastasis of the spinal cord tumor.

Immunohistochemistry was performed using the Envision polymer method (Dako Japan Co. Ltd., Kyoto, Japan). The
following antibodies were used as primary antibodies; rabbit antisera against human glial fibrillary acidic protein (GFAP, Prediluted, Dako), bovine galactocerebroside (GC, 1:200, Chemicon, Temecula, CA, U.S.A.), bovine S-100 (1:400, Dako), myelin basic protein (MBP, prediluted, Zymed Laboratories, South San Francisco, CA, U.S.A.) and neuron-specific enolase (NSE, 1:200, Dako), and mouse monoclonal antibodies against human neurofilament (NF, 1:20, Dako).
vimentin (1:40, Dako), synaptophysin (1:20, Dako), and proliferating cell nuclear antigen (PCNA, prediluted, Dako). To visualize microglia, sections were stained with biotinylated lectin Ricinus communis agglutinin-1 (RCA-1, 1:400, EY Laboratories, San Mateo, CA, U.S.A.). The lectin staining was done using the avidin-biotin peroxidase complex method (Vector Laboratories, Burlingame, CA, U.S.A.). Immunohistochemically, neoplastic round cells with abundant clear cytoplasm and small lymphocyte-like cells were completely negative for GFAP. Only a few of GFAP-positive astrocytes were recognized within the neoplastic foci (Fig. 6), and many GFAP-positive astrocytes were distributed at the periphery. Immunostaining for MBP and GC labeled myelin sheaths and intact oligodendrocytes intensely, and intact and reactive astrocytes also showed moderate immunoreactivity for GC. Neoplastic round cells were moderately positive for GC and negative for MBP. The neoplastic cells were negative for other antibodies, including NF, synaptophysin, vimentin, S-100, NSE, and lectin RCA-1. The number of tumor cells with PCNA-positive nuclei was very small, approximately 3 to 5 cells per high-power magnification (10×40). A similar number of PCNA-positive astrocytes were detected at the periphery of the neoplastic foci. The results of PCNA staining indicate a poor growth activity of the neoplastic cells.

Typically oligodendroglioma forms soft gelatinous mass, occasionally containing cystic spaces and leptomeningial or ventricular extension is quite common [2, 8, 14]. Histopathologically, this tumor is characterized by a honeycomb appearance formed by accumulation of tumor cells with artificially swollen clear cytoplasm and central nuclei [9, 12, 13]. Several immunohistochemical markers such as MBP, GC, and Leu 7, have been applied for diagnosis of human oligodendrogliomas [10, 12], although the findings have varied from case to case. These previous studies indicated there were no specific markers for the diagnosis of oligodendrogliaomas. Moreover, the co-presence of GFAP-positive cells in oligodendrogliaomas [4, 6] becomes problematic when trying to differentiate pure oligodendroglioma from mixed glioma (oligo-astroglioma).

The present spinal tumor had the histological characteristics of typical oligodendrogloma reported in humans and several animal species [9, 12, 13]. The tumor showed a honeycomb appearance formed by accumulation of round cells with vacuolated cytoplasm, and these neoplastic cells were negative for GFAP. Cystic spaces containing small round neoplastic cells, were prominent in this tumor. In both human and animal oligodendrogliomas, similar cystic changes have been commonly described, and are considered to occur by mucinous degeneration of the tumor [9, 12, 13, 15]. Based on these morphological features, the present case was diagnosed as oligodendrogloma. Recently, it has been reported that some brain tumors including astrocytoma, ependymoma, or central neurona, can occasionally exhibit honeycomb-like structures [3, 7]. However, the negative immunoreactivity of the tumor for GFAP, NSE, NF and synaptophysin may support our diagnosis. A few GFAP-positive astrocytes were present in the neoplastic foci, and diffuse proliferation of GFAP-positive astrocytes was recognized at the tumor periphery. These GFAP-positive astrocytes were considered to be reactive astrocytes. The presence of a sub-population of neoplastic cells with astrocytic differentiation known as minigemistocytes or glio-fibrillary oligodendrocytes has been demonstrated in many human oligodendrocytic tumors [4, 11]. However, we were unable to confirm the neoplastic nature of the GFAP-positive cells in the present case. Since histopathological differentiation between pure oligodendroglioma and mixed glioma (oligo-astroglioma) may be quite difficult, mixed glioma could still be considered in the differential diagnosis of this tumor. Anaplastic (malignant) oligodendrogliomas are characterized by anaplastic morphology and prominent mitotic activity of tumor cells, vascular endothelial proliferation, and abundant necrosis sometimes with calcium deposits [9, 12, 13]. In spite of the wide arachnoidal dissemination, the tumor cells showed the typical morphology of oligodendrogloma with low growth activity, suggested by the extreme rarity of mitotic figures and PCNA immunoreactivity. Moreover, endothelial proliferation, necrosis, and calcification were not prominent in the present tumor. Thus, these morphological features are thought to be quite different from those of anaplastic oligodendrogloma.

Although there are few reports of spinal oligodendrogliomas in animals [5, 15], the spinal white matter may be affected. Even in humans spinal oligodendrogliomas are described as rare, and most cases have arisen in children [2, 8, 14]. Radiation therapy is considered to be effective for this tumor, but many cases have a poor clinical prognosis. Nam et al. [8] mentioned that the poor prognosis of spinal oligodendrogloma might be due to its biological nature frequently showing wide extension or dissemination. In their review, Fortuna et al. [2] cited several articles in which intracranial or spinal meningeal extension of oligodendrogloma known as “oligodendroglomatosis”, was reported as frequent, seven of 10 necropsied cases showing pathological evidence for this event. In oligodendrogliomas of animals, similar biological features have been emphasized [13], although such findings might be based mainly on canine cerebral oligodendrogliomas, including anaplastic oligodendrogliomas. In the present case, diffuse arachnoidal dissemination of the tumor cells was found in the subarachnoidal space from the 2nd lumbar to 3rd sacral levels of spinal cord, in spite of the well differentiated morphological features and low mitotic activity. Since diffuse invasion of neoplastic cells in the subarachnoidal space was recognized at the primary site, tumor seeding might have occurred easily and widely to the lower part of the spinal cords through the cerebrospinal fluid. These findings indicate that bovine spinal oligodendrogloma has similar biological characteristics to that of the human form. It is difficult to appraise the clinical features of the present
tumor, although the wide subarachnoidal dissemination indicates a poor prognosis, as in human cases.

REFERENCES