The Journal of Veterinary Medical Science

NOTE

Pathology

Canine intracranial meningioma with rosette-like collagen deposits

Ryo SAITO[1)], James K. CHAMBERS[1)]*, Yoshiki SUGIYAMA[2)] and Kazuyuki UCHIDA[1)]

[1)]Laboratory of Veterinary Pathology, Graduate School of Agricultural and Life Sciences, The University of Tokyo, Tokyo, Japan
[2)]Uminonakamichi Animal Clinic, Fukuoka, Japan

J. Vet. Med. Sci.
84(6): 766–769, 2022
doi: 10.1292/jvms.22-0074

Received: 21 February 2022
Accepted: 19 April 2022
Advanced Epub:
28 April 2022

ABSTRACT. A 13-year-old female Miniature Dachshund showed seizures and an intracranial mass was seen in the left temporal lobe. Three months after first surgical resection, a recurrence lesion was recognized. Histopathologically, proliferation of spindle cells with diffuse rosette-like eosinophilic deposits, which stained blue with Masson's trichrome stain, was observed. In electron microscopy, the rosette-like deposits were consisted of bundles of minute filaments which were assumed to be collagenous fibrils. Immunohistochemically, the neoplastic cells were positive for vimentin and cytokeratin, and negative for E-cadherin, S100, glial fibrillary acidic protein (GFAP), oligodendrocyte transcription factor (Olig2), and CD204. The rosette-like collagen deposits were positive for type 4 collagen and negative for type 1 collagen. In this report, we describe histopathological features of a canine meningioma with the rosette-like collagen deposits.

KEYWORDS: brain, collagen, dog, meningioma, rosette

In brain tumors, rosette formation is typically observed in ependymomas, which originate from ependymal cells covering the ventricular system [6]. Homer-Wright rosette observed in primitive neuroectodermal tumors (PNET) or neuroblastomas is histopathologically similar to the rosette of ependymomas, excluding that Homer-Wright rosette doesn't contain blood vessels [6]. Furthermore, meningiomas with the rosette-like deposits were reported in human and a dog [3, 5, 7–10]. These deposits stained blue with Masson's trichrome stain, and the collagenous deposits in human meningioma were positive for type 1 collagen [3, 5, 7–10]. However, histopathological and immunohistochemical features of the tumor cells and the rosette-like deposits are not well known, especially in dogs. The lack of histopathological knowledge of meningiomas with the rosette-like deposits can lead to misdiagnosis of these brain tumors despite their different prognosis. In this report, we describe the knowledge of intracranial tumors with rosette or rosette-like construct formation and histopathological features of a canine meningioma with the rosette-like deposits by histological examination, electron microscopy, and immunohistochemistry.

A 13-year-old female Miniature Dachshund showed seizures and an intracranial mass (2.1 × 2.0 × 2.3 cm) was seen in the left temporal lobe by the computed tomography (CT) and magnetic resonance imaging (MRI, Fig. 1). After the first resection, the dog was treated with antibiotics and antiepileptics, that is phenobarbital (3 mg/kg, twice per day), levetiracetam (30 mg/kg, 3 times per day), glyceol (20 cc, twice per day), isobide syrup (4 cc, twice per day). Three months after first surgical resection, a recurrence lesion (0.8 × 0.8 × 1.5 cm) was recognized by the CT and MRI. Second surgical resection was performed two more months later. Although administration of antibiotics and antiepileptics, such as zonisamide (18.75 mg, twice per day) and diazepam, was continued, the patient showed seizures 65 days and died 136 days after the second resection. At the time of first and second surgery, the intradural extramedullary mass was resected. On gross examination, the mass was white and solid. The boundary between the mass and brain parenchyma was clear.

For histological examination, both masses resected at first and second surgery were fixed in formalin and sent to the Laboratory of Veterinary Pathology, Graduate School of Agricultural and Life Sciences, the University of Tokyo. These masses had the same characteristics in the histopathological and immunohistochemical analyses. Histopathologically, proliferation of spindle neoplastic cells with diffuse rosette-like eosinophilic deposits, which did not contain blood vessels, was observed adjacent to the meninges (Fig. 2). The rosette-like deposits were consisted of radial eosinophilic substances and were surrounded by the neoplastic cells. Brain parenchyma and dural invasion of neoplastic cells were observed in first occurrence. In 10 high power fields (2.37 mm^2), the mitotic figures of neoplastic cells were 1 and 5 in first and second tissues, respectively. Furthermore, the rosette-like deposits

*Correspondence to: Chambers, J. K.: achamber@mail.ecc.u-tokyo.ac.jp, Laboratory of Veterinary Pathology, Graduate School of Agricultural and Life Sciences, The University of Tokyo, 1-1-1 Yayoi, Bunkyo-ku, Tokyo 113-8657, Japan

stained blue with Masson's trichrome stain and were assumed to be collagen fibers (Fig. 3). The deposits were also positive for periodic acid-Schiff (PAS) stain.

For electron microscopy, small pieces of formalin-fixed samples obtained in the second resection were refixed in 1% osmium tetroxide in 0.1 M phosphate buffer and then embedded in epoxy resin. Ultra-thin sections were stained with uranyl acetate and lead citrate and examined using a transmission electron microscope (JEM-1400Plus, JEOL, Tokyo, Japan). The rosette-like deposits were consisted of bundles (1.5 micrometer in diameter) of minute filaments which were assumed to be collagenous fibrils (Fig. 4).

Immunohistochemistry was performed using the primary antibodies in Table 1. The antibodies were validated by a positive reaction in canine brain tissues. As negative controls, each primary antibody was replaced by an irrelevant antibody. After reaction with the primary antibodies, the sections were incubated with anti-mouse or anti-rabbit Envision horseradish peroxidase-labelled polymer (DAKO, Tokyo, Japan) at 37°C for 40 min. Finally, the reactions were visualized with 0.05% 3-3′-diaminobenzidine and 0.03% hydrogen peroxide in Tris-hydrochloric acid buffer, followed by a counterstain with Mayer's hematoxylin. Immunohistochemically, the neoplastic cells were diffusely positive for vimentin (Fig. 5) and cytokeratin (Fig. 6), and negative for E-cadherin, S100, glial fibrillary acidic protein (GFAP), oligodendrocyte transcription factor (Olig2), and CD204. The rosette-like collagen deposits were positive for type 4 collagen (Fig. 7) and negative for type 1 collagen (Fig. 8).

The rosette-like deposits observed in the present case were revealed to be consisted of type 4 collagen fiber. Considering the nature of the rosette-like deposits and the immunohistochemical results of the neoplastic cells, the dog was diagnosed with meningioma with collagen fiber deposits and its recurrence lesion.

In the present case, the rosette-like eosinophilic deposits, which stained blue with Masson's trichrome stain, were diffusely observed and blood vessels were not observed in these structures. These features were different from that of the rosette structures observed in ependymoma, PNET, and neuroblastoma [6].

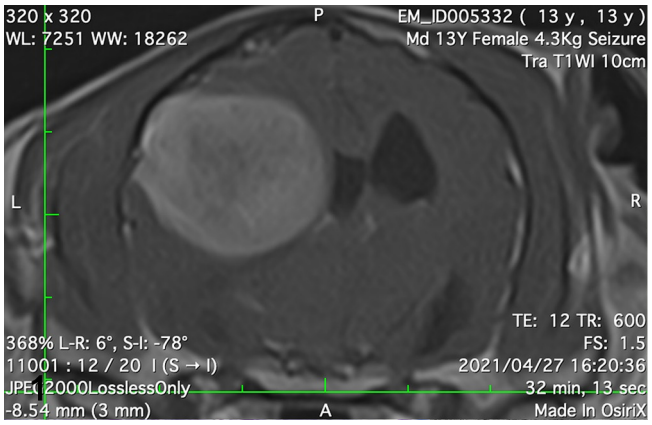

Fig. 1. Heterogeneously strong tumor enhancement in the contrast-enhanced T1-weighted imaging.

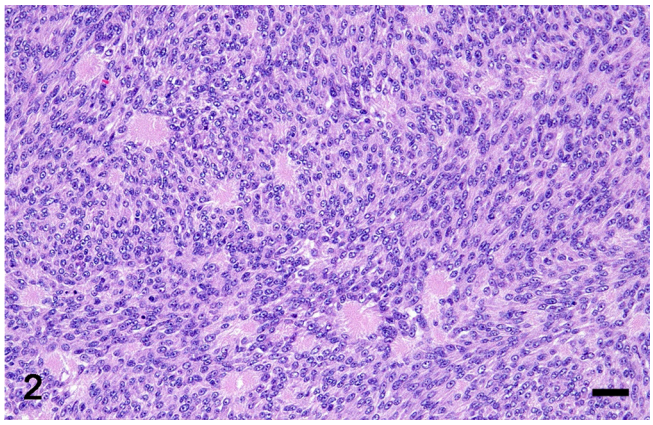

Fig. 2. Spindle neoplastic cells with rosette-like eosinophilic deposits. Hematoxylin and eosin. Bar=50 µm.

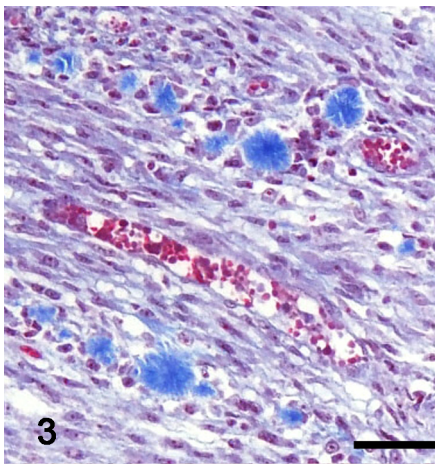

Fig. 3. The rosette-like deposits stains blue with Masson's trichrome stain. Bar=50 µm.

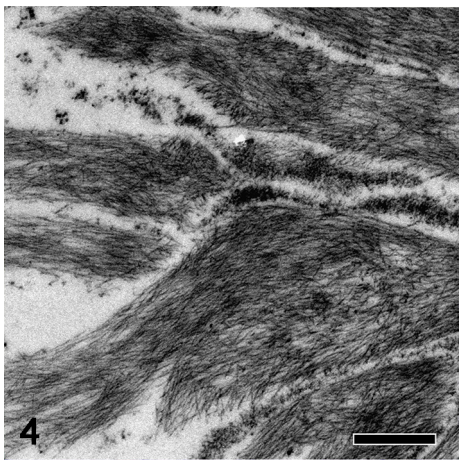

Fig. 4. The rosette-like deposits consist of bundles of minute filaments. Electron microscopy. Bar=2 µm.

Table 1. Primary antibodies used for immunohistochemical analysis

	Host (clone)	Dilution	Antigen retrieval	Source	Catalog no.	Positive cells
Vimentin	Mouse (V9)	Ready to use	121°C, 10 min, pH 6.0	Dako, Tokyo, Japan	IR630	Microglia
Cytokeratin	Mouse (AE1/AE3)	Ready to use	121°C, 10 min, pH 6.0	Dako	IR053	Epithelium cells (skin)
E-cadherin	Mouse (36/E-cadherin)	1:1,000	121°C, 10 min, pH 9.0	BD Biosciences, Franklin Lakes, NJ, USA	610182	Meningeal cells
S100	Rabbit	1:500	None	Dako	Z0311	Neural cells
Gfap	Mouse (1G4)	1:1,000	121°C, 10 min, pH 6.0	Dako	Z0334	Astrocytes
Olig2	Rabbit	1:500	121°C, 10 min, pH 9.0	Millipore, Burlington, MA, USA	AB9610	Oligodendrocytes
Cd204	Mouse (SRA-E5)	1:25	121°C, 10 min, pH 9.0	Transgenic, Fukuoka, Japan	KT022	Microglia
Type 1 collagen	Mouse (COL-1)	1:1,000	Proteinase K, 20 min, 0.125 mg/ml	Abcam, Cambridge, UK	ab6308	Connective tissue
Type 4 collagen	Rabbit	1:500	Proteinase K, 20 min, 0.125 mg/ml	Abcam	ab6586	Blood vessels

GFAP, glial fibrillary acidic protein; Olig2, oligodendrocyte transcription factor.

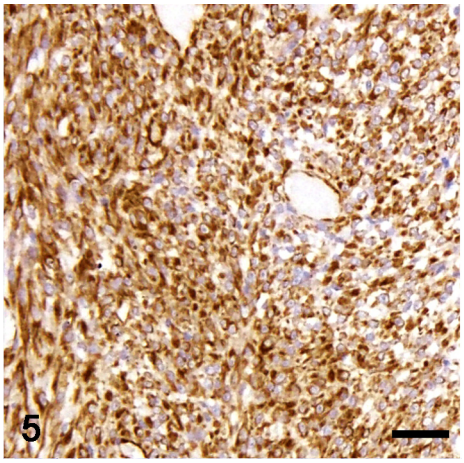

Fig. 5. Neoplastic cells are diffusely and strongly immunolabeled for vimentin. Immunohistochemistry for vimentin. Bar=50 µm.

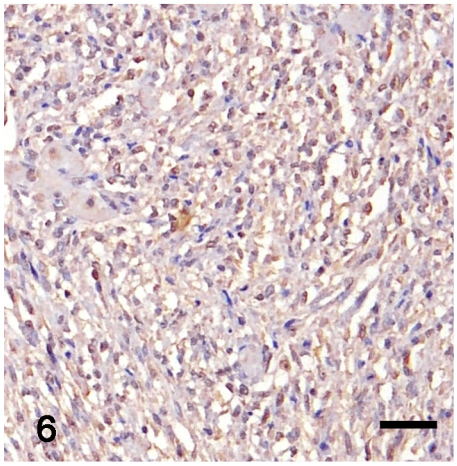

Fig. 6. The neoplastic cells are scattered and weakly immunolabeled for cytokeratin AE1/AE3. Immunohistochemistry for cytokeratin AE1/AE3. Bar=50 µm.

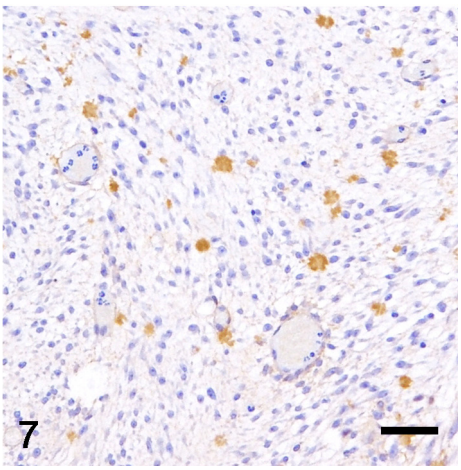

Fig. 7. The rosette-like deposits are immunolabeled for type 4 collagen. Immunohistochemistry for type 4 collagen. Bar=50 µm.

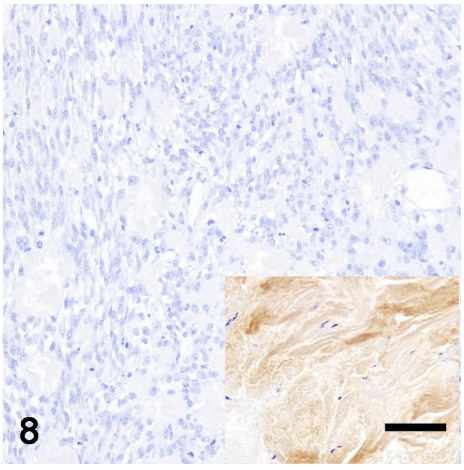

Fig. 8. The rosette-like deposits are negative for type 1 collagen. Inset: positive control (connective tissue of the present case) for type 1 collagen. Immunohistochemistry for type 1 collagen. Bar=50 µm.

The rosette-like deposits in this case were identified to be consisted of collagen fibers by electron microscopy. Furthermore, immunohistochemistry revealed the deposits were consisted of type 4 collagen which constitutes basal membrane. These results indicated that the neoplastic cells in this case had type 4 collagen productivity. In the brain, meningothelial cells are the unique cell population which produce type 4 collagen [1]. Therefore, the neoplastic cells were assumed to be meningeal origin. The immunohistochemical results also indicated their meningeal origin, that is the neoplastic cells were positive for cytokeratin and vimentin, and negative for glial, neural and histiocytic markers, including S100, GFAP, Olig2, and CD204.

A previous study suggested that human meningioma with collagenous rosette formation should be classified to grade 1 and showed collagen deposits were positive for collagen 1 [3]. However, the neoplastic cells of the present case were negative for E-cadherin and brain invasion was observed in the primary tumor, which is the characteristic of high grade meningiomas [2, 4]. Considering the immunohistochemical results, tumor recurrence, and brain parenchyma invasion, the present case was classified to grade 2, atypical meningioma. Furthermore, the rosette-like collagen deposits were positive for type 4 collagen, and not for type 1 collagen. To the best of our knowledge, the only case of canine meningioma with the rosette-like collagen deposits was a secretory meningioma [8]. Human meningiomas with the rosette-like deposits show various histopathological morphology and classified to several histological subtypes [5, 7, 9, 10]. Therefore, rosette-like collagen deposit can be observed in various subtypes of meningiomas. As for discordance of the collagen type produced in the present and previous study, there may be two possibilities. One is species difference between dog and human. The other is that various types of collagens can be produced in human and canine meningioma with the rosette-like deposits. In any case, more research about the characteristic of the collagen produced in meningioma with the rosette-like deposits will be required because immunohistochemical examination was performed in the present and only one previous study [3].

As for the intracranial tumors, rosette or Homer-Wright rosette formation is typically observed in ependymomas, PNET and neuroblastomas [6]. However, meningiomas also form the rosette-like collagen deposits as the present and previous studies showed [3, 5, 7–10]. To the best of our knowledge, this is the first report which performs histopathological and immunohistochemical examination on a canine intracranial meningioma with the rosette-like deposits in detail and clarifies the characteristics of the deposits.

DECLARATION OF CONFLICTING INTERESTS. The authors have no conflicts of interest with respect to the authorship or the publication of this article.

ACKNOWLEDGMENTS. We thank Dr S. Kimura for his excellent technical assistance for electron microscopy. The authors received no financial support for the study and/or authorship of this article.

REFERENCES

1. Decimo, I., Fumagalli, G., Berton, V., Krampera, M. and Bifari, F. 2012. Meninges: from protective membrane to stem cell niche. *Am. J. Stem Cells* **1**: 92–105. [Medline]
2. Figarella-Branger, D., Roche, P. H., Daniel, L., Dufour, H., Bianco, N. and Pellissier, J. F. 1997. Cell-adhesion molecules in human meningiomas: correlation with clinical and morphological data. *Neuropathol. Appl. Neurobiol.* **23**: 113–122. [Medline] [CrossRef]
3. Haybaeck, J., Smolle, E., Schökler, B. and Kleinert, R. 2016. The WHO Grade I collagen-forming meningioma produces angiogenic substances. A new meningioma entity. *Anticancer Res.* **36**: 941–949. [Medline]
4. Ide, T., Uchida, K., Suzuki, K., Kagawa, Y. and Nakayama, H. 2011. Expression of cell adhesion molecules and doublecortin in canine anaplastic meningiomas. *Vet. Pathol.* **48**: 292–301. [Medline] [CrossRef]
5. Liverman, C., Mafra, M., Chuang, S. S., Shivane, A., Chakrabarty, A., Highley, R., Hilton, D. A., Byrne, N. P., Wesseling, P. and Perry, A. 2015. A clinicopathologic study of 11 rosette-forming meningiomas: a rare and potentially confusing pattern. *Acta Neuropathol.* **130**: 311–313. [Medline] [CrossRef]
6. Meuten, D. J. 2017. Tumors of the nervous system. pp. 834–891. In: Tumors in Domestic Animals, 5th ed. (Higgins, R. J. ed.), Wiley-Blackwell, Hoboken.
7. Poyuran, R., Thomas, B., Abraham, M. and Narasimhaiah, D. 2020. Meningioma with rosettes: a rare morphologic pattern. *Neuropathology* **40**: 202–205. [Medline] [CrossRef]
8. Schöniger, S., Woolford, L., Jutras, L., Head, E., de Lahunta, A. and Summers, B. A. 2013. Unusual features in four canine meningiomas. *J. Comp. Pathol.* **149**: 237–241. [Medline] [CrossRef]
9. Tada, T., Ishii, K., Oshima, S., Hara, H. and Kobayashi, S. 1992. Secretory meningioma associated with numerous meningothelial rosettes. *Acta Neuropathol.* **84**: 342–345. [Medline] [CrossRef]
10. Vaidya, M. M., Shenoy, A. S. and Goel, N. A. 2019. Meningiomas with collagenous rosettes: a report of three cases. *Asian J. Neurosurg.* **14**: 568–570. [Medline] [CrossRef]