Ganglioneuroma in the Urinary Bladder of a Dog

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ABSTRACT. An 11-year-old male Labrador retriever presented with chronic oliguria. Ultrasonography findings revealed a protruding mass at the neck of the urinary bladder. A cystotomy was performed, and the mass was removed by ligation with surgical sutures. Histopathological examination revealed conspicuous foci with a variable number of ganglion cells in the tumor and abundant interwoven bundles of schwannian cells with fine fibers. The ganglion cells were positive for neuron-specific enolase and neurofilament. The schwannian cells were positive for vimentin, S-100 protein, and glial fibrillary acidic protein. Thus, according to the classification of neuroblastic tumors, which are uncommon tumors of nerve cell origin, are classified into neuroblastoma, ganglioneuroblastoma, and ganglioneuroma depending on the degree of maturation of neoplastic neuroblasts and development of schwannian stroma [5, 6, 15]. In dogs, ganglioneuroblastoma and ganglioneuroma have been reported at various sites such as the jejunum [12], rectum [2, 11], olfactory cavity [8], thoracic area [14], oral mucosa [9], and central nervous system [7, 13]; however, to our knowledge, there has been no reports on neuroblastic tumors in the urinary bladder of dogs. Here, we describe the histopathological and immunohistochemical findings of a ganglioneuroma in the urinary bladder of an adult dog.

An 11-year-old male Labrador retriever was admitted to an animal hospital with repetitive oliguria. There were no abnormal findings in general condition, routine physical examinations and blood test results. Ultrasonography showed a protruding mass at the neck of the urinary bladder. At cystotomy, there was a solitary tumor of polypoid structure connecting to the bladder wall by narrow stalk at the trigone area. Since locating the tumor near the urethral opening, it was removed by ligation with surgical sutures. The dog did not develop a recurrent neoplasm or metastasis after surgery.

The tumor was fixed in 10% neutral-buffered formalin, embedded in paraffin through a standard procedure, sectioned, and stained with hematoxylin and eosin (HE) and with cresyl violet solution for the detection of Nissl substances. The serial sections were stained using the peroxidase-conjugated immune polymer method (Envision; Dako, Glostrup, Denmark) with rabbit anti-neuron-specific enolase (NSE) polyclonal antibody (Dako), mouse anti-human neurofilament (NF) monoclonal antibody (Dako), rabbit anti-bovine S-100 protein polyclonal antibody (Dako), mouse anti-vimentin monoclonal antibody (Dako), and rabbit anti-glial fibrillary acidic protein (GFAP) polyclonal antibody (Dako). The sections for immunohistochemistry were deparaffinized, immersed in a target antigen retrieval solution (Dako) at 121°C for 20 min, developed in diaminobenzidine solution (Dako), and then counterstained with Mayer’s hematoxylin.

The tumor was 2.5 × 1.0 cm in size, firm, white, and demarcated at the cut surface, and the overlying urinary mucosa was intact. Histopathological examination revealed conspicuous foci with a variable number of ganglion cells and abundant interwoven bundles of spindle cells in the submucosal area. The spindle cells were elaborated fine fibers and considered to be schwannian cells. The present tumor was shared by those two particular components, the ganglion cells and schwannian cells, approximately 80–90% of the tissue (Fig. 1A and 1B). The ganglion cells had a large, stellate to polygonal cytoplasm and large nuclei with prominent nucleoli. There was a various amount of Nissl substances in the cytoplasm which revealed purple by cresyl violet stain (Fig. 1C). In addition, there were small spindle-shaped condensed cells around the ganglion cells, which resembled the satellite cells. The ganglion cells were variable in size up to 50 µm, occasionally binucleated, and distributed solitarily or in small clusters. The ganglion cells in the small clusters were considerably small with none or indistinct Nissl substances in the cytoplasm. They are considered to be at the premature stage. The ganglion cells, being either solitarily as in cluster, were encompassed by schwannian cells in the deep area of the tumor mass, while no association with schwannian cells for those in the super-
ficial area. The ganglion cells stained positive for NSE (Fig. 1D) and NF (Fig. 1E), whereas the schwannian cells stained positive for vimentin, S-100 protein, and GFAP (Fig. 1F).

Ganglioneuromas are composed primarily or exclusively of the ganglioneuromatous component, whereas ganglion-neuroblastomas consist of an admixture of ganglioneuromatous and neuroblastomatous components; generally, the ganglioneuromatous component is present in an excess of 50% of the tumor [4, 15]. In contrast to these two tumors, neuroblastomas are predominantly composed of neuroblastomatous components. Thus, ganglioneuromas are the most differentiated in all neuroblastic tumors. In our case, the tumor consisted of ganglioneuromatous components, including mature and immature ganglion cells and prolifer-
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Atning schwannian cells, but the distinct neuroblasticomatous nests were not observed in any area; therefore, we diagnosed the tumor as a ganglioneuroma. Similar to human ganglioneuroma, canine ganglioneuroma has a favorable prognosis [3, 4, 11, 12]. In our case, the tumor recurrence and metastasis were not observed after surgery as reported in previous cases [3, 4, 11, 12], thus ganglioneuroma is a benign tumor.

Peripheral neuroblastic tumors are considered to originate from the progenitor cells of the neural crest, and not as a result of the dedifferentiation of mature ganglion cells [9, 15]. In the urinary bladder of an adult dog, there are many intramural ganglia, which are almost choline acetyltransferase-positive parasympathetic ganglia [1, 10]. These intramural ganglia are present as clusters of immature ganglion cells in the subserosal area in the early fetal stages [1]. It is possible that the ganglioneuroma of the urinary bladder originate from these primitive neuronal tissues.

Ganglioneuroma and ganglioneuroblastoma have been reported in various organs; however, to the best of our knowledge, this is the first report of ganglioneuroma in the urinary bladder of a domestic animal.

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