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NOTE

Pathology

Lingual ganglioneuroma in a dog

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ABSTRACT. A mass was found at the base of the dorsum linguae of a male 11-year-old Labrador retriever. The tumor comprised of ganglion cells and Schwannian cells with Verocay bodies. The ganglion cells were positive for neuron-specific enolase, S-100, nerve growth factor receptor, and beta III tubulin. The Schwannian cells were positive for neuron-specific enolase, S-100, nerve growth factor receptor, and glial fibrillary acidic protein. The lingual mass was diagnosed as a ganglioneuroma. To our knowledge, there has been no previous report of a lingual ganglioneuroma in a dog.

KEY WORDS: dog, ganglioneuroma, tongue

Tumors of peripheral neurons can be classified into ganglioneuromas, ganglioneuroblastomas, and neuroblastomas [1]. Ganglioneuromas comprised of well-differentiated dense Schwannian cells and variously distributed ganglion cells [6]. Ganglioneuromas are previously reported in dogs, cats, pigs, and goats [4]. In dogs, ganglioneuromas have been reported to occur in the jejunum [13], rectum [14], skin of the thoracic area [3], and urinary bladder [15]. Ganglioneuroblastomas have been reported in the olfactory epithelium [10], thoracic area [16] and oral mucosa [12]. To our knowledge, there has been no previous report of a lingual ganglioneuroma in a dog.

A mass was found incidentally on the tongue of an 11-year-old male Labrador retriever during intubation for resection of right upper and left lower palpebral Meibomian adenomas. The tumor was located in the dorsal base of the tongue, and had a pedunculated papillary shape (Fig. 1). It measured 2.5 × 2.5 × 3.0 cm in with a white, solid and rubbery cut surface. Despite the existence of this mass, no obvious clinical signs were observed.

The resected tumor was fixed with 10% neutral buffered formalin, embedded in paraffin, sectioned, and stained with hematoxylin and eosin. Nissle stain with cresyl violet and immunohistochemistry were also performed on serial sections. Serial sections for immunohistochemistry were heated for 15 min at 121°C in a target retrieval solution (pH6.0, Dako, Glostrup, Denmark) and incubated overnight at 4°C with the following primary antibodies: rabbit anti-bovine S-100 polyclonal antibody (pre-diluted, Nichirei, Tokyo, Japan), rabbit anti-neuron-specific enolase (NSE) polyclonal antibody (1:10,000, Millipore, Billerica, MA, U.S.A.), mouse anti-nerve growth factor receptor (NGFR) monoclonal antibody (1:200, Leica biosystems, Newcastle, U.K.), rabbit anti-glial fibrillary acidic protein polyclonal antibody (1:100, Dako, Glostrup, Denmark), mouse anti-beta III tubulin monoclonal antibody (1:10,000, Promega, Madison, WI, U.S.A.), and mouse anti-Ki-67 monoclonal antibody (1:50, Dako, Glostrup, Denmark). The positive reactions in sections were visualized with 3, 3′-diaminobenzidine solution (Liquid DAB+ substrate-chromogen system, Dako, Glostrup, Denmark) and counterstained with hematoxylin (Hematoxylin 3G, Sakura finetek Japan, Tokyo, Japan). As positive controls, normal dog brain tissue sections were used for NSE, S-100, NGFR, beta III tubulin and glial fibrillary acidic protein, and normal dog skin tissue section was used for Ki-67. As a negative control, primary antibody was omitted.

On histopathological examination, the tumor was poorly demarcated, with infiltrative growth in the submucosa, and comprised of abundant interwoven bundles of spindle-shaped mesenchymal cells and aggregated or scattered ganglion cells. The spindle cells were elongated, with thin and wavy nuclei, and were morphologically identified as Schwann cells. Verocay bodies, formed by two compact rows of well-aligned nuclei separated by fibrillary cell processes, were also scattered in the tumor (Fig. 2). The ganglion cells contained Nissl bodies which stained positively with cresyl violet and were accompanied by small, spindle satellite cells which had condensed nuclei and little cytoplasm. A few ganglion cells had two nuclei (Fig. 3). There was no cellular atypia in the

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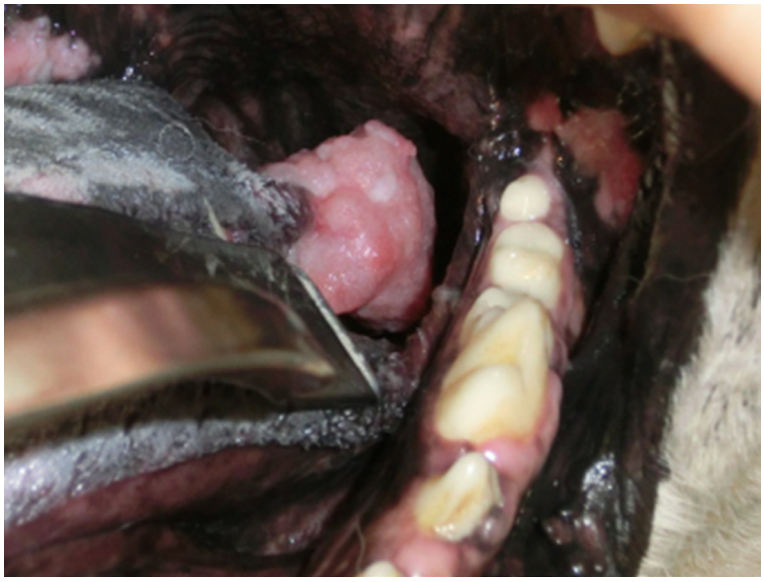

Fig. 1. Gross morphology of the lingual tumor. A mass located on the dorsal aspect of the base of the tongue.

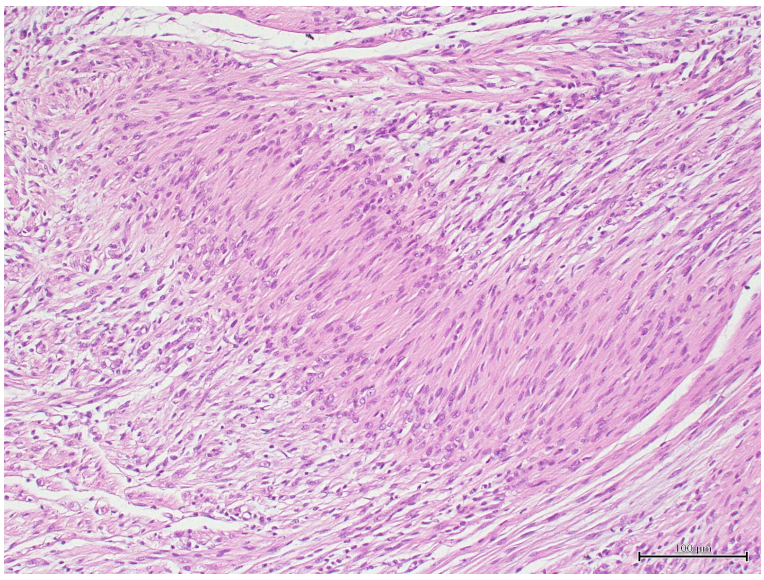

Fig. 2. Histopathology of the lingual tumor. There were many Verocay bodies in the tumor lesion. Hematoxylin and eosin stain; bar, 100μm.

ganglion or Schwann cells, except for binucleation in ganglion cells, and no mitotic figures were detected. Immunohistochemically, the spindle and satellite cells were positive for NSE, S-100, glial fibrillary acidic protein, and NGFR, consistent with Schwann cells (Fig. 4). The ganglion cells were positive for NSE, S-100, NGFR and beta III tubulin. Axons labeled focally or filamentously with antibody against beta III tubulin were observed. There were very few (<1%) or no Ki-67-positive cells in the Schwann and ganglion cell population, respectively.

Because the tumor in the present case was composed of Schwannian cells and ganglion cells, differential diagnoses included other neuroblastic tumors, peripheral nerve sheath tumor, traumatic neuroma associated with pre-existing ganglia [8], and ganglioneuromatous hamartoma [5]. Histologically, the Schwannian cells proliferated in bundles, and formed Verocay bodies, suggesting that these Schwannian cells were neoplastic. Additionally, the ganglion cells were also considered to be neoplastic cells, because these cells not only aggregated, but were also bi-nucleated in the present case. Because of the presence of both neoplastic schwannian cells and ganglion cells, ganglioneuromatous hamartoma, peripheral nerve sheath tumor and traumatic neuroma were excluded from diagnosis. Moreover, there were no neuroblasts in any area of the tumor, no proliferative ganglion cells, or Ki-67-positive cells, suggesting that the ganglion cells were fully mature. The tumor was consequently diagnosed as ganglioneuroma based on the classification of human and domestic animals neuroblastic neoplasms [1, 6]. Unfortunately, information of

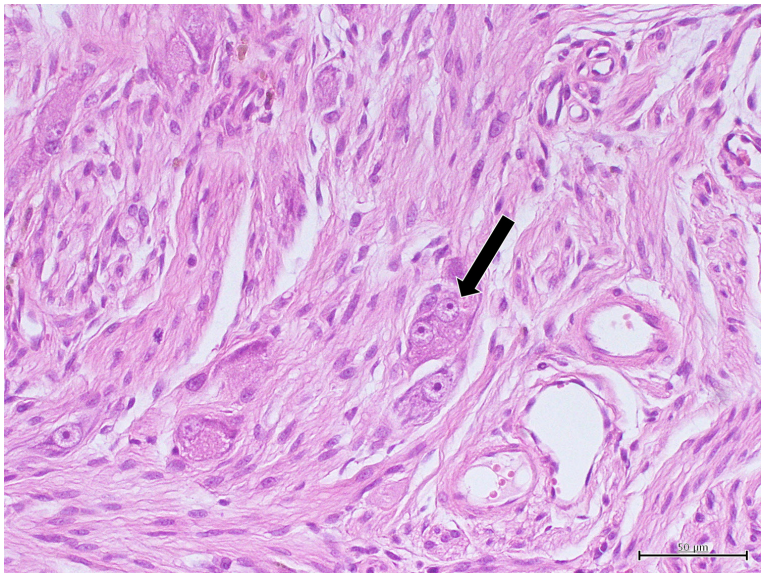

Fig. 3. Histopathology of the lingual tumor. There were also binucleated ganglion cells (arrow). Hematoxylin and eosin stain; bar, 50 μm.

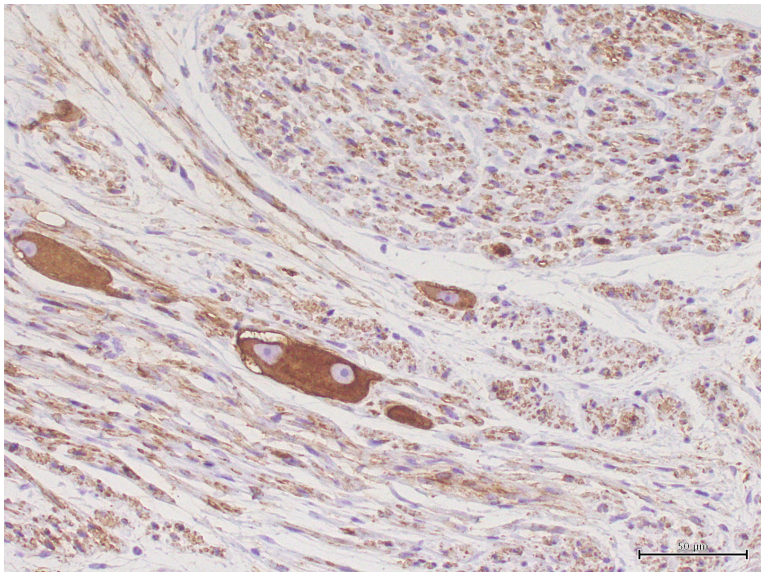

Fig. 4. Immunohistochemical stain of the lingual tumor. The ganglion cells and spindle cells were positive for NGFR in the cytoplasm. Immunohistochemistry, bar, 50 μm.

clinical outcome of the present case was unavailable. However, since the surgical margin of neoplastic tissue was clear and ganglioneuroma is a benign tumor, the prognosis of the present case is considered good [3, 4, 14].

Peripheral neuroblastic tumors are considered to originate from the progenitor cells of the neural crest [17]. A case of human ganglioneuroma on the base of the tongue similar to the present case has been previously reported [9]. In the human tongue, ganglia exist in the lateral margin or just below the taste buds, in the subepithelial nerve plexus [11], although, this area is an unusual site of ganglioneuromas [9]. In contrast, dogs have hemiganglia in the base of the vallate papillae and foliate papillae, which are located in the base of the dorsal tongue [2, 7]. Therefore, in the present case, we considered that the tumor was derived from the subepithelial nerve plexus of these papillae.

In conclusion, although ganglioneuromas and other neuroblastic tumors have been reported in various organs, to our knowledge, the present case is the first report of a lingual neuroblastic tumor in a dog. We believe that the findings of the present case may aid in the differential diagnoses of similar cases in the future.

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