NOTE *Surgery*

Maxillofacial Rhabdomyosarcoma in the Canine Maxillofacial Area

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ABSTRACT. Three dogs had a diagnosis of maxillofacial rhabdomyosarcoma. These dogs were treated with surgery and/or radiotherapy, and had poor clinical responses. The tumor tissues in all three cases were observed around the upper premolar teeth with ulcerative lesions and CT examinations in each case revealed extensive bony involvement into the maxilla. Two cases were subjected to surgical excision of the tissues, followed by an external radiation therapy. The other case was only treated with palliative radiation. Outcomes of the treatment of all the cases were quite poor because of the invasive and refractory nature of the tumor cells, leading to the local recurrence and lung metastasis early in the clinical course. All dogs died within two months of the first admission.
KEY WORDS: canine, oral tumor, rhabdomyosarcoma.

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Rhabdomyosarcomas are one of the soft tissue sarcomas seen in the veterinary field [12]. Cardiac, laryngeal, and bladder are predisposing portions of canine rhabdomyosarcomas, and several reports on this tumor have been published [1, 5–7, 9, 10, 13, 15, 16]. Although the number of cases has been quite limited, rhabdomyosarcoma has been reported to sometimes occur in the canine oral cavity [3, 8, 11]. In this paper, we report three cases of canine rhabdomyosarcoma in the canine oral cavity, located around the upper premolar teeth, which resulted in poor prognosis because of their refractory behavior to treatment and distant metastasis observed in the early clinical course.

Case 1 was a male 10-year-old mix-breed dog and was presented to the veterinary teaching hospital of Yamaguchi University with a 2-week-history of a swelling of the left maxillofacial area. A hard mass was observed beneath the left eye, but no gross lesion was seen in the gingival tissue of the oral cavity at first admission (Fig. 1A). CT examination revealed a mass lesion invading maxilla, suggestive of a malignant oral tumor. Thoracic radiography showed no metastatic lesions. The owner of the dog did not expect surgical treatment after the first diagnosis. However, the lesion had rapidly enlarged and neoplastic tissue could be observed around the upper premolar teeth, 11 days after the first admission (Fig. 1B), therefore, surgical resection was scheduled. The mass was removed with a partial maxillectomy without severe complications and a submandibular lymph node was removed as it appeared swollen. A recovery from surgery was unremarkable. The mass was histopathologically diagnosed as a rhabdomyosarcoma.

Post-operative radiation therapy was conducted because the mass had grown rapidly before surgery and also seemed highly invasive. During radiation treatment regimen, however, the general physical condition of the dog decreased. Thoracic radiography revealed a thoracic effusion (Fig. 2). Malignant tumor cells were detected from the effusion, suggestive enough of lung metastasis. The dog died 29 days after surgery owing to respiratory distress.

Case 2 dog was a male 10-year-old golden retriever with a 2-week-history of a swelling of the left maxillofacial area that closely resembled the case 1 dog in appearance. Neoplastic tissue around the upper premolar teeth could be identified in the oral cavity (Fig. 1C). In the CT examination, a large mass as well as a defect in the maxilla was observed (Fig. 3). A submandibular lymph node was palpable. A biopsy on the lesion was performed, which revealed that the mass was a rhabdomyosarcoma. Cytological evaluation of the submandibular lymph node suggested tumor invasion. Pre-operative radiation of 3 fractions of 4Gy were delivered to the tumor but no effect was observed. Since the owner of

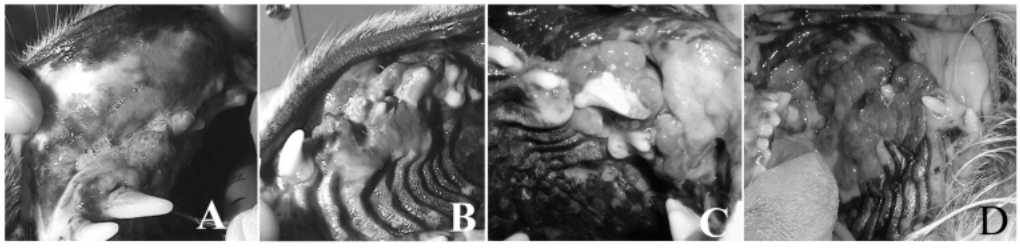

Fig. 1. Gross appearances of tumor tissues in three dogs. A: Case 1 dog at first diagnosis, B: Case 1 dog at the 11th day after the first diagnosis, C, D: Case 2 and 3 dogs at first diagnosis, respectively.

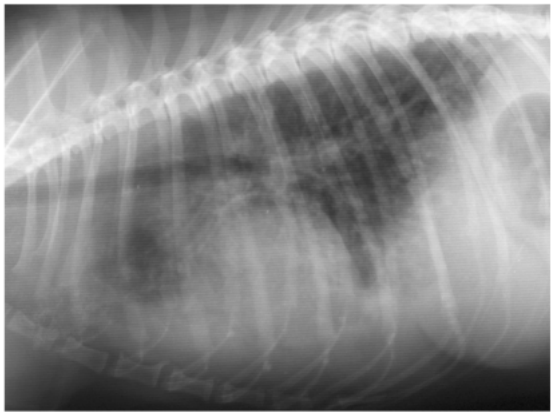

Fig. 2. Thoracic radiograph of the Case 1 dog. Thoracic effusion was evident.

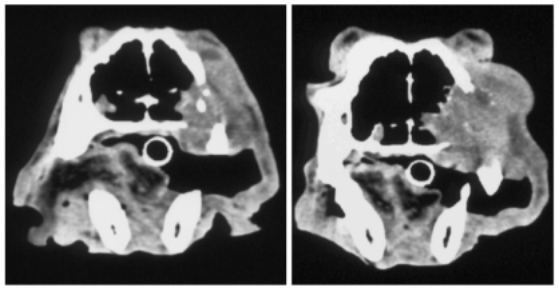

Fig. 3. CT findings of the Case 2 dog. The tumor tissues invaded into the nasal cavity, destroying the maxilla.

the dog hoped for a surgical removal of the mass, a partial maxillectomy was conducted which successfully removed the mass lesion. The submandibular lymph nodes were also removed. Recovery from surgery was uneventful.

After surgery, post-operative radiation continued, and a further 7 fractions of 4Gy were delivered to the surgical site in order to prevent recurrence. However, the thoracic radiography taken at the last fraction suggested diffuse lung metastasis. The dog also presented difficulty in opening its mouth, possibly due to tumor recurrence around the temporomandibular joint. The owner did not ask for further treatment, and the dog died 2 months after first admission.

Case 3 was a male 12-year-old Shih-tuz that was presented to our hospital with the neoplastic ulcerative lesion in the right upper premolar area, which had already diagnosed histopathologically as a rhabdomyosarcoma in the referring veterinary hospital, 1 month before the admission (Fig. 1D). The aim of visiting our hospital was palliative radiation. In the CT evaluation of the lesion, the maxilla just under the lesion disappeared, and the neoplastic tissue had invaded into the nasal cavity and orbital area through the defect. An incisional biopsy of the lesion was done again, which resulted in rhabdomyosarcoma. A submandibular lymph node showed a slight swelling. No metastatic lesion was suspected by thoracic radiography.

Radiation therapy was conducted, and the dog was treated with 40 Gy in 4 Gy fractions over 5 weeks. After the first

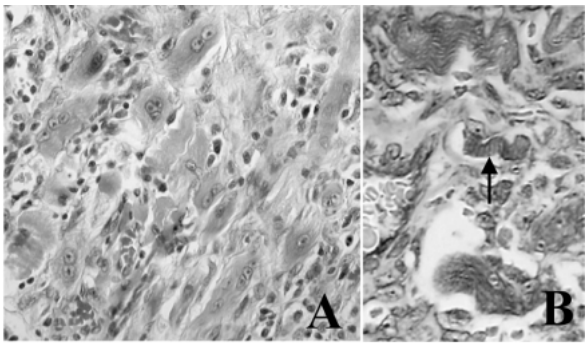

Fig. 4. Typical histopathological findings of the tumor tissue from the Case 2 dog. A: The tumor cells with eosinophilic cytoplasms were roughly arranged (× 400, HE stain), B: Cross striation (arrow) was observed in the tumor cell (× 650, PTAH stain).

treatment, the tumor showed some changes in color, became less reddish suggesting some effect of radiation on the tumor. But no further obvious changes could be observed. After the 10th treatment, a thoracic radiography of the dog suggested lung metastasis. The owner of the dog did not expect any further treatment. The dog died at home two weeks after that.

Typical histopathological findings of the cases were shown in Fig. 4. The tumor tissue in the surgical specimens contained loosely arranged and fleshy cells. The nuclei of the cells were hyperchromatic and cytoplasms were deeply eosinophilic (Fig. 4A). These characteristics of the tumor cells were compatible with those of rhabdomyoblasts. In phosphotungstic acid-hematoxylin (PTAH) staining, cross-striations within cytoplasms were observed in some tumor cells (Fig. 4B). These cytological features were essentially common to three cases, and suggested that these tumors were rhabdomyosarcomas.

Rhabdomyosarcomas are malignant neoplastic diseases, derived from striated cells in skeletal muscles. In human medicine, this tumor is a common soft tissue sarcoma in childhood and much information on diagnosis and treatment of this malignancy is available [2, 14]. About 40% of human rhabdomyosarcomas are believed to arise in the head and neck region, and a further 25% in the genitourinary tract [14]. In the veterinary field, on the other hand, canine rhabdomyosarcomas have been reported less frequently in comparison to human medicine, and predisposing sites of the tumor seem to differ from human cases. Laryngeal and cardiac rhabdomyosarcomas have been known to occur in dogs, as well as one developing in the bladder, known as a botyroid tumor [1, 5–7, 9, 10, 13, 15, 16]. Other studies on the canine cases observed the tumor in the tongue [3, 11]. However, the rhabdomyosarcoma developing in the oral gingival tissue as described in this paper was rarely reported. In one previous report, two rhabdomyosarcoma cases in canine gingival tissue and the oropharynx area were described [8]. We encountered three cases of rhabdomyosarcoma developing in the maxillofacial area. These three

cases showed a close resemblance in the developing location of the upper premolar area, as well as in poor clinical courses. Since there has been quite limited information on rhabdomyosarcoma in the canine oral cavity, incidences of the tumor remained unclear, but we should consider this kind of the tumor as a differential histopathological type of canine malignant oral tumors. The muscle tissues of the origin of these tumors also remained unclear, however Musculus levator labii maxillaries and/or Musculus caninus might be the possible origin of the tumors.

Prognosis of rhabdomyosarcoma in the oral cavity, including the tongue, seemed to be poor. Most of the previous cases showed rapid growth, regional lymph node involvement, tumor recurrence after surgery, and distant metastasis [3, 8, 11]. Also in our report, the rapid growth of the tumor tissue included invasion into the maxilla, even in the early clinical course, as a common characteristic in these three cases. In CT examination, all cases showed the destruction of the bony tissues adjacent to the tumors, which suggested the malignant nature of the tumor, and pulmonary metastasis was observed in all the cases. In order to give an appropriate prognosis, a histopathological examination of the tissue is required before starting treatment.

Human rhabdomyosarcomas have been treated by multimodal therapy including surgery, chemotherapy and radiotherapy. According to large scale studies on human rhabdomyosarcoma, recent advances in these multimodal therapies have attributed to the improvement of outcomes [2, 14]. Canine soft tissue sarcomas have also been treated with various treatment forms, mainly consisting of surgery and radiation treatment [4, 12]. In this series, two cases were treated surgically, which could reduce the tumor volume. Surgery has been considered to be a mainstay for the treatment of soft tissue sarcomas. Considerations for taking a wide margin have been emphasized whenever surgery is conducted for soft tissue sarcomas. In the case 2 dog however, the tumor tissue showed regrowth caudal to the primary lesion after surgery. It was difficult to apply wide margins because of the advanced clinical stage as well as anatomical problems of the oral cavity. Furthermore, the swelling of the regional lymph nodes were observed at first admission, suggestive of the aggressive nature of the tumor cells. These findings indicated that the surgery alone would not be an appropriate treatment form against canine oral rhabdomyosarcoma.

Radiation therapy was conducted in all three dogs; two were postoperative, and the other was treated by radiation alone. In general, post-operative radiation has been considered acceptable treatment form after incomplete excision of soft tissue sarcomas [4, 12]. However, efficacy of radiation to the oral rhabdomyosarcoma is questionable. Post-operative radiation seemed less effective because the tumor showed rapid regrowth in the case 2 dog. Furthermore, in the case 3 dog, the tumor tissue showed only a slight degenerative change after radiation. Although the number of cases was quite limited, canine oral rhabdomyosarcoma appeared resistant to radiation.

Survival durations of these three cases were quite unsatisfactory. All dogs died within two month of first admission. In contrast to several descriptions on canine soft tissue sarcomas stating these tumors rarely metastasized [12], lung metastasis or thoracic effusion evident in the thoracic radiographs might be fatal in all the dogs, although none were necropsied. The data suggest that the distant metastasis can be considered to have established early in the clinical course of the disease, and therefore, systemic chemotherapy should be scheduled in order to eliminate potential micrometastaic diseases. Chemotherapy is essential in the treatment of human rhabdomyosarcomas; all patients with rhabdomyosarcoma were subjected to chemotherapy with the aim of local control of the disease, as well as to prevent developing distant metastastic lesions [2, 14]. Combinations of antineoplastic drugs, such as vincristine, dactinomycin, and cyclophosphamide, have been the mainstay of chemotherapy [2, 14]. In treating canine soft tissue sarcoma, however, the role of chemotherapy has still remained unclear. We did not use chemotherapeutic drugs in our three cases, but further clinical applications of chemotherapy against canine rhabdomyosarcoma might be required as a systemic treatment form.

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