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Successful Carboplatin Chemotherapy for Oral Fibrosarcoma in the Buccal Mucosa of a Dog

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Abstract : An 11-year-old castrated male cocker spaniel presented with halitosis, anorexia, and swelling of the left face. Upon physical examination, a firm mass was detected in the left buccal mucosa. Fine needle aspiration cytology revealed a malignant tumor of mesenchymal origin. We performed biopsy, which gave a diagnosis of oral fibrosarcoma. The client refused surgical treatment, and carboplatin chemotherapy (300 mg/m^2, IV, q 21 days) was initiated. The mass gradually decreased in size and disappeared about 89 days after the initial chemotherapy. Complete remission was attained, and the tumor did not relapse. This case report shows that a single carboplatin chemotherapy session can achieve macroscopic complete remission of oral fibrosarcoma.

Key words **:** carboplatin, dog, oral fibrosarcoma.

Introduction

The oral cavity is a common region for the development of malignant and benign cancers (10,11,16). Most cancers affecting the oral cavity have an unclear etiology. Oral cancer accounts for about 6-7% of all canine cancers and is the fourth most common cancer overall (10,14,16). Oral malignant melanoma, oral squamous cell carcinoma (SCC), and oral fibrosarcoma are the 3 most common oral tumors in dogs (10,16). Other malignant canine oral tumors include osteosarcoma, chondrosarcoma, anaplastic sarcoma, multilobular osteochondrosarcoma, intraosseous carcinoma, myxosarcoma, hemangiosarcoma, lymphoma, and mast cell tumors (1,3,4,9-12,16). The treatment of choice for rostrally located tumors is surgery, radiation therapy, or a combination of both (2,8,10,11). The role of chemotherapy in the treatment of oral tumors has not been defined clearly. However, several studies on the treatment of oral tumors were recently reported (1,3,5,7,10,12,14,15).

In this report, we describe a successful chemotherapy with carboplatin in a case of canine oral fibrosarcoma.

Case

An 11-year-old castrated male English cocker spaniel presented with halitosis, anorexia, and swelling of the left face. The patient had been managed with a cyclooxygenase (cox)-2 inhibitor (celecoxib, 2 mg/kg, PO, q 12 hours) (Celebrex®; Pfizer Phamaceuticals Korea, Korea) for a few months because of mild intervertebral disk disease (IVDD). Physical examination revealed a 2.5 × 2 cm firm mass with erosion and hemorrhage in the left buccal mucosa (Fig 2-A).

The result of complete blood count was within the reference range. Serum biochemical profiles revealed mildly elevated alkaline phosphokinase. Skull, thorax, and abdominal radiography showed no remarkable findings.

The results of fine needle aspiration cytology of the oral mass demonstrated numerous spindle cells, multinucleation of cells, marked pleomorphism of cell size, anisokaryosis, anisocytosis, prominent multiple nucleoli, and variable nuclear-to-cytoplasmic ratio (Fig 1-A). Thus, a malignant tumor of mesenchymal cell origin was strongly suspected. We performed biopsy, and a definite diagnosis of oral fibrosarcoma was made on the basis of histopathological examination (grade I). Histologically, the tumor cells composed of pleomorphic spindle-shaped cells and formed intertwining bundles and occasional whorls (Fig 1-B and C).

The client refused surgical resection and instead selected chemotherapeutic treatment. Therefore, we administered carboplatin (300 mg/m^2, IV, q 21 days) (Carbotinol®; Korea United Pham., Korea) to the patient. The size of the oral mass decreased gradually after chemotherapy, and macroscopic complete remission was attained 89 days after the initial chemotherapy (Fig 2). Three months after chemotherapy, the oral lesion disappeared completely and chemotherapy was stopped (total number of chemotherapy treatments: 4 times). The oral tumor did not relapse for 2 years after chemotherapy, but the dog eventually died of natural causes.

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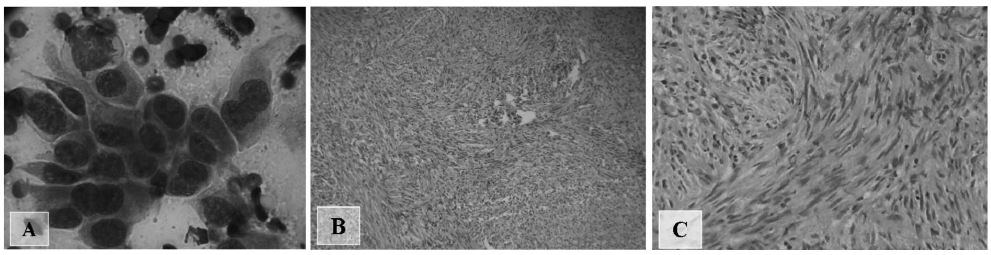

Fig 1. FNA (A) and histopathological (B) findings of the present case. A: Numerous spindle shaped cells and multinucleated cells are revealed on FNA cytologic examination. Malignant mesenchymal cell origin tumor is strongly suspected. B (× 200, H & E stain) and C (× 400, H & E stain): Oral fibrosarcoma is definitely diagnosed based on histopathological examination.

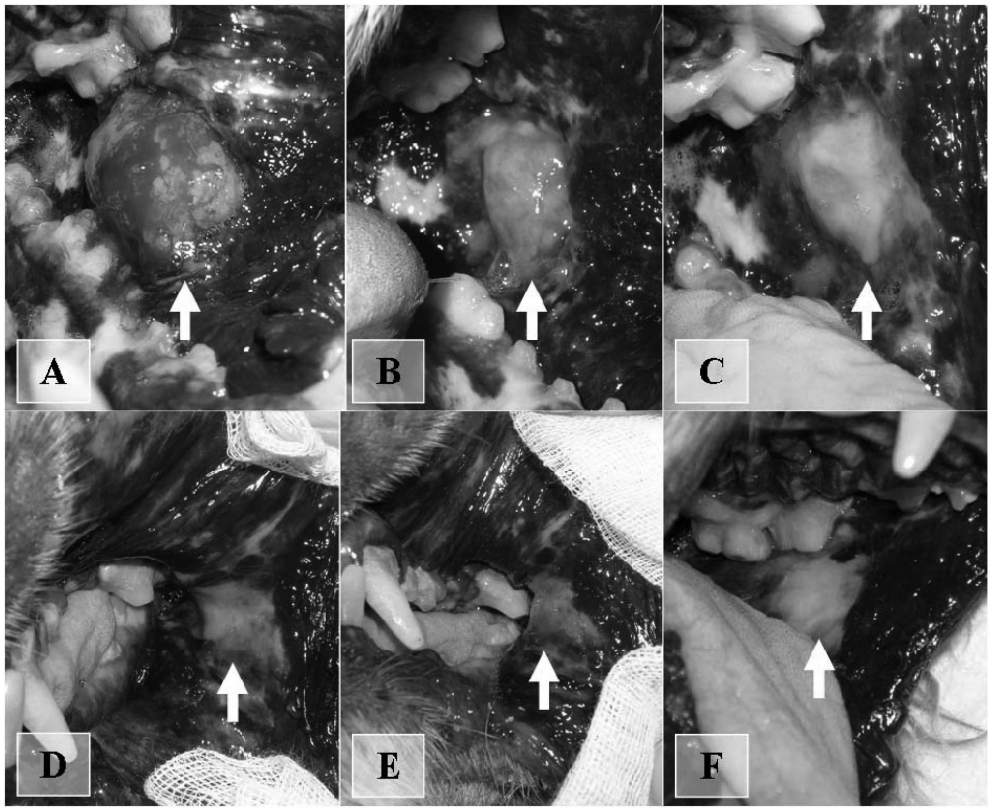

Fig 2. Serial gross findings of oral fibrosarcoma lesion after chemotherapy in the present case (A: before chemotherapy, B: 26 days after chemotherapy, C: 46 days after chemotherapy, D: 51 days after chemotherapy, E: 74 days after chemotherapy, F: 89 days after chemotherapy). The firm mass with erosion and hemorrhage on left buccal mucosa is observed on initial day (A). Size of the mass is decreased gradually after chemotherapy and macroscopic complete remission is detected 89 days after chemotherapy.

Discussion

According to previous reports (1,3,9,14), administration of cox-2 inhibitors in canine oral SCC and oral melanoma has beneficial antitumor effects. Cox-2 is an induced enzyme and is expressed by cells that are involved in inflammation and other pathological conditions such as cancer (9). One study (9) indicated that cox-2 expression was observed in canine oral SCC and melanoma. However, the cox-2 protein was not detected in canine oral fibrosarcoma. Thus, in contrast to cases of oral SCC or melanoma, cox-2 inhibitors could not prevent disease progression or induce remission in oral fibrosarcoma cases. For that reason, the present patient contracted oral fibrosarcoma while being managed with a cox-2 inhibitor for a few months because of mild IVDD.

Definitive therapy for oral tumors consists of surgical removal, radiation therapy, chemotherapy, or a combination of 2 or more methods (10,11,16). Although the survival time of patients with oral fibrosarcoma is longer than those with oral squamous cell carcinoma and melanoma after surgical resection, oral fibrosarcoma is locally aggressive and commonly shows recurrence after surgical treatment (10,11). According to a previous report (11), two-thirds of patients with oral fibrosarcoma survived more than 2 years after surgical

treatment. However, most of these fibrosarcoma cases had recurrences within the survival times. Furthermore, according to our experiences, most clients may decline aggressive surgical procedures such as mandibulectomy. Radiation therapy is a beneficial treatment option to prevent recurrences after surgical resection, but this might be expensive.

Carboplatin and doxorubicin have shown beneficial effects against soft tissue sarcomas in veterinary medicine (6,7,10,15). Carboplatin is a second-generation platinum compound and is a widely used chemotherapeutic agent with demonstrated activity against numerous solid tumors in human medicine. However, clinical reports describing the use of carboplatin in spontaneous tumors in veterinary medicine are limited (6,12, 13). In one previous report (12), carboplatin showed a measurable response in 28% of dogs with malignant melanomas. Recently, several studies were reported on chemotherapy with carboplatin alone or carboplatin with doxorubicin for osteosarcoma in small animals (4,13,15). However, due to the low number of cases reported, the beneficial effects of chemotherapy on oral fibrosarcoma were not fully evaluated. Few studies have evaluated the use of chemotherapeutic agents for dogs with oral fibrosarcoma (5,7). In one previous study (7), 3 cats with oral fibrosarcoma were treated with cyclophosphamide and doxorubicin. One cat showed a complete remission for 5 months and another cat showed partial remission (greater than 50%) for 2 months. However, tumors regrew at 5 and 2 months after chemotherapy in the two cats, respectively. The third cat showed no response to chemotherapy, but the tumor did not grow for 7 months. In another previous report (5), complete clinical remission of an oral fibrosarcoma in a cat treated with vincristine lasted for 10 months. In the present patient, oral fibrosarcoma showed complete clinical remission after carboplatin chemotherapy and the tumor did not relapse for 2 years.

This case report demonstrates that chemotherapy with carboplatin alone can achieve macroscopic complete clinical remission of oral fibrosarcoma. Therefore, carboplatin chemotherapy could be a clinically useful therapeutic option for treating oral fibrosarcomas in animals for which surgical treatment is not an option.

To the author's knowledge, this is the first report of a successful chemotherapy with carboplatin in canine oral fibrosarcoma.

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개의 구강점막에 발생한 구강 섬유육종에서 카보플라틴의 성공적인 항암치료 효과

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요 약 : 11년 령의 중성화된 수컷 코커 스파니엘견이 구취, 식욕부진과 좌측 안면부의 부종 증상을 보여 내원하였다. 신체 검사 상에서 좌측 구강점막의 단단한 종괴가 확인되었다. 가는 침 흡인 세포검사 결과 악성의 중간엽 유래 종양이 가장 의심되어 생검을 실시하였고 조직검사 결과 섬유육종으로 진단되었다. 보호자의 거부로 수술적인 치료가 아닌 카보플라틴 (carboplatin, 300 mg/m^2, IV, q 21 days)을 이용한 항암치료를 실시하였다. 항암치료 시작 후 육안적으로 종양의 크기가 현저히 줄어들어 약 89일 후에는 육안적으로 완전 경감되었다. 총 4회의 항암치료 이후 항암치료를 중단하였고 종양의 재발은 일어나지 않았다. 본 증례보고는 개의 구강 섬유육종에서 carboplatin을 이용한 항암 치료가 육안적인 종양의 완전 경감을 유도할 수 있음을 보여준다.

주요어 : 카보플라틴, 개, 섬유육종