A Multicentric Squamous Cell Carcinoma of the Oral Cavity in a François's Leaf Monkey (*Trachypithecus francoisi francoisi*)

Miya UEDA¹⁾, Hiroko SOMURA²⁾, Kirito MATSUI¹⁾, Rei MATSUMOTO¹⁾,
Yasuhiko YAMAMOTO²⁾ and Kanji TAMAI²⁾

1) Yokohama Zoological Gardens, 1175-1 Kamishiranecho, Asahi-ku, Yokohama,
Kanagawa 241-0001, Japan

2) Former — Yokohama Zoological Gardens

(2006 年 11 月 14 日受領, 2007 年 8 月 1 日採択)

フランソワルトンにみられた多中心性口腔扁平上皮癌の一例

植田美弥¹⁾, 草村弘子²⁾, 松井桐人¹⁾, 松本令以¹⁾, 山本裕彦²⁾, 玉井勘次²⁾

1) 横浜市立よこはま動物園 〒241-0001 横浜市旭区上白根町 1175-1

2) 元横浜市立よこはま動物園

ABSTRACT. A multicentric squamous cell carcinoma was found in the oral cavity of an adult female François's leaf-monkey (*Trachypithecus francoisi francoisi*). The monkey showed apparent swelling of the facial region, and physical examinations revealed gingival swelling and osteolysis of both the mandible and maxillary region. Incisor regions of the maxillary and mandibular bones were replaced by neoplastic tissue, and a white nodule was found on the right cervical lymph node. Histopathological examinations revealed that the neoplasm was composed of multiple variably-sized islands of malignant neoplastic squamous epithelial cells with metastasis to the right cervical lymph node. This is the first report of oral squamous cell carcinoma in a leaf-monkey reared at a Japanese zoo.

Key words: Squamous cell carcinoma, Oral cavity, François's leaf monkey

Jpn. J. Zoo. Wildl. Med. 12(2) : 117-121, 2007

Squamous cell carcinoma is the most commonly reported spontaneous neoplasm of the oral cavity of nonhuman primates. It has evoked great interest due to the fact that the anatomic and physiological features of the nonhuman primates most closely resemble those of man [1]. In a recent overview of world literature, 34 out of 39 reported cases of oral or esophageal squamous cell carcinoma in nonhuman primates, occurred in macaques and 5 in squirrel monkeys (*Saimiri sciureus*) [1]. Squamous cell carcinoma of the oral cavity was also reported in an infant cynomolgus monkey in Japan [2]. Four additional cases of the carcinoma have been reported in the oral cavity of squirrel monkeys [3,4,5,6]. In this study, we report a spontaneous squamous cell carcinoma in the oral cavity of an adult female François's leaf-monkey (*Trachypithecus francoisi francoisi*) reared at Yokohama Zoological Gardens in Japan.

François's leaf-monkey is distributed from the northern part of Vietnam to the southern part of mainland China. This typical leaf-eater is considered to be facing a high risk of extinction in the wild. In the IUCN Red List [7], François's leaf-monkey is classified in the "Vulnerable" category.

The monkey examined in this study was female and estimated to be 12 years old. She came to Japan from the Shanghai Zoo in 1999, and gave birth in 2002 and 2005.

In September 2005, she showed apparent swelling of the facial region with purulent nasal secretion (Fig. 1). One month later, physical examinations including radiography revealed prominent gingival swelling of both mandibles and maxillary region associated with osteolysis of the maxillary and mandibular bones (Fig. 2). The upper incisors showed slight displacement, and the lower and upper incisors were found to be loose. After performing biopsy of gingival tissue, her clinical condition took a sudden turn for the worse on 15th October, 2005, and she died the next day.

The animal was routinely necropsied and all organs were fixed in 10% phosphate-buffered (pH 7.2-7.3) formalin. The heart, liver, spleen, kidney, alimentary tract, cervical lymph node and gingival lesions were embedded in paraffin, and 4 to 5 μ m sections were stained with hematoxylin and eosin.

Macroscopically, the incisor regions of the maxillary and mandibular bones were replaced by the neoplastic tissue. The enlargement was also observed on the floor of the oral cavity and gingival region (Fig. 3). The right cervical lymph node became swollen and was replaced with neoplastic tissue in the cut surface. Intestinal invagination was observed at the small intestine, and the mucus membrane of small intestine showed extensive reddening.

Histopathological examinations showed that the neoplasm of

Miya Ueda et al.

Fig. 1 Showing apparent swelling of the facial region.

Fig. 2 Lateral radiograph of the skull demonstrating osteolysis of the maxillary and mandibular bones (arrows).

Squamous cell carcinoma in a leaf monkey

Fig.3 Gross feature of the mandible. Note the apparent swelling of the gingival region and the floor of the oral cavity (arrows).

the oral cavity was composed of multiple variably-sized islands of neoplastic squamous epithelial cells (Fig. 4). Cells in the central regions of the lobules were undergoing keratinization and forming large central cores of keratin, the so-called "cancer pearls" (Fig. 4). The neoplastic cells were well-differentiated squamous epithelial cells characterized by large vesicular nuclei with prominent, darkly basophilic nucleoli, brightly eosinophilic cytoplasm, and conspicuous intercellular bridges (Fig. 5). Mitotic indices of the neoplastic cells in the maxillary and mandibular regions were 26/10 HPF (High-Powered Fields) and 14/10 HPF, respectively. At the edge of the neoplasm, some free tumor cells were observed, indicating that the tumor extended to the adjacent tissue. The tumor cells were frequently observed to invade the lymphatic vessels. Morphological characteristics of the neoplastic tissue found in the mandibular bone corresponded exactly to that in the maxillary bone.

The white nodule in the cervical lymph node consisted of metastatic neoplasm with apparent cancer pearls (Fig. 6). Severe hemorrhage was observed in the submucosa of the small intestine. However, no inflammatory cellular response was prominent in the hemorrhagic area. Small necrotic foci without visible microbial invasions were very few in the liver. There were no remarkable lesions in the heart, spleen and kidney.

From the histopathological features, this case was diagnosed as a spontaneous squamous cell carcinoma, most likely originating from the floor of the oral cavity or gingiva. Severe hemorrhage of the small intestine was likely to be caused by intestinal invagination, and reflected the possibility of hypovolemic shock, which may have played an important role in the acute death of this case. The focal necrosis found in the

liver parenchyma was not considered to correlate with the neoplastic lesions. The hepatic lesions might have been caused by some infectious agents, but this could not be confirmed in the present study.

Most oral squamous cell carcinomas of nonhuman primates were reported to possess a history associated with draining bone sinuses, surgical debridement, reparative epulis, halitosis or loose teeth [3,4,5,6]. Especially, draining bone sinuses and reparative epulis are well recognized as factors related to human oral squamous cell carcinoma [8,9]. However, we could not find any predisposing or relating factors in this case of squamous cell carcinoma. Given the clinical history and histopathological features, it was likely that the neoplastic tissues found in the maxillary and mandibular regions of the present case were multicentric. To our knowledge, multicentric squamous cell carcinoma of the oral cavity has not been reported in non-human primates to date. Although some multicentric squamous cell carcinomas have been reported in human patients [10, 11], they occurred in the female lower genital tract. Therefore, it appears that pathogenesis of the present case would be exceedingly rare. This is the first case of oral squamous cell carcinoma in François's leaf-monkey reared at Japanese zoo.

要 約

フランソワルトン成獣雌の多中心性口部扁平上皮癌症例を経験した。本例は顔面の腫大がみられ、上下顎部の歯肉の腫大と顎骨の吸収像が確認された。剖検の結果、上下顎切歯部は腫瘍性組織に置換され、右頸部リンパ節には白色結節が観察された。病理組織学的に顎部には扁平上皮癌が様々な大きさの島状構造

Miya Ueda et al.

Fig. 4 Neoplastic lesion is composed of multiple variably sized islands (black arrows) of neoplastic squamous epithelial cells. Cancer pearls are prominent (white arrow).

Fig. 5 The neoplastic cells (arrows) are characterized by large vesicular nuclei with a single, prominent, darkly basophilic nucleolus, and brightly eosinophilic cytoplasm.

Squamous cell carcinoma in a leaf monkey

Fig. 6 Metastatic lesion in the cervical lymph node with apparent cancer pearls (arrows).

を呈して認められ、右頸部リンパ節には転移像がみられた。本例は我が国の動物園飼育ルン類における口部扁平上皮癌の初報告である。

REFERENCE

1. Beniashvili DS. 1989. An overview of the world literature on spontaneous tumors in nonhuman primates. *J Med Primatol* 18: 423-437.
2. Nakamura S, Sakakibara I, Ono F, Shibata S, Michishita M, Ishii Y, Kobayashi R, Takahashi K, Yoshikawa Y. 2000. Squamous cell carcinoma of the oral cavity in an infant cymonolgus monkey. *Exp Anim* 49: 225-228.
3. Kluver H, Brunshwig A. 1947. Oral carcinoma in a monkey colony. A report on two additional cases. *Cancer Res* 7: 627-633.
4. Sasseville VG, Pauley DR, Spaulding GL, Chalifoux LV, Lee-Parritz D, Simon MA. 1993. A Spontaneous squamous cell carcinoma of the oral cavity in a squirrel monkey (*Saimiri sciureus*). *J Med Primatol* 22: 272-275.
5. Morris TH. 1994. A further case of squamous cell carcinoma in the oral cavity of a squirrel monkey. *J Med Primatol* 23: 317-318.
6. Montesdeoca D, Roberts J, Donnelly TM. 1992. Asymmetry of the face of a squirrel monkey. Squamous cell carcinoma of the oral cavity. *Lab Anim* 21: 18-21.
7. IUCN 2004. *2004 IUCN Red List of Threatened Species*. IUCN, Gland, Switzerland.
8. Horn CV, Templeton AC. 1971. Carcinoma developing in a draining sinus of chronic osteomyelitis of the humerus. *Brit J Surg* 58: 399-400.
9. Inglis AM, Morton KS, Lehmann ECH. 1979. Squamous cell carcinoma arising in chronic osteomyelitis. *Canad J Surg* 22: 271-273.
10. Feng Q, Kiviat NB. 2005. New and surprising insights into pathogenesis of multicentric squamous cancers in the female lower genital tract. *J National Cancer institute* 97: 1798-1799.
11. Sengupta S, Das JK, Gangopadhyay A. 2005. Multicentric squamous cell carcinoma over lesions of porokeratosis palmaris et plantaris disseminata and giant porokeratosis. *Indian J Dermatol Venereol Leprol* 71: 414-416.