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Spontaneous Squamous Cell Carcinomas in 13 Baboons, a First Report in a Spider Monkey, and a Review of the Nonhuman Primate Literature

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Abstract

Background—Squamous cell carcinoma (SCC) is a neoplastic proliferation of epithelial cells undergoing squamous differentiation and represents a diagnostic challenge in nonhuman primates (NHP), especially in baboons with perineal SCC.

Methods—Fourteen SCC (13 baboons, 1 spider monkey) were identified over a 20-year period. A literature search identified 86 additional published cases of spontaneous NHP SCC.

Results—SCC was most commonly reported in macaques, baboons, marmosets, and squirrel monkeys. Metastasis occurred in 23%, of NHP. The most frequently reported primary locations were the oral cavity, integument, esophagus, and cervix-uterus. Perineal SCC occurred mainly in baboons. All reported SCC in marmosets occurred in the head. Nasal cavity SCC was only reported in male marmosets. All reported pulmonary SCC occurred in males, mostly in tree shrews.

Conclusions—SCC is a common neoplasm in NHP and exhibits species differences. NHPs may provide a useful SCC animal model.

Keywords

Cancer; neoplasm; *Papio*; skin; oral cavity; esophagus

Introduction

Squamous cell carcinoma (SCC) is a neoplastic proliferation of epithelial cells undergoing squamous differentiation, and is a common tumor in nonhuman primates (NHP). SCC is the most common neoplasm of the oral cavity [5,13,14,39], esophagus [5] or skin and perineum [5,14] in several reviews, and was commonly reported in a survey of 11 zoos and NHP facilities [43]. Grossly, SCC typically appears as nodular and irregular proliferations of firm tissue, frequently with ulceration, local invasion into adjacent soft tissues and bone, or occasional metastasis to regional lymph nodes. Histologically, keratin pearls, intercellular bridges, cytokeratin positivity and invasiveness are characteristics of SCC.

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Predisposing factors for the development of SCC include sun exposure and chronic irritation [1,53]. An association between SCC and papillomavirus infection has also been reported in humans [16], NHP [71,72], and cats [1]. SCC has been induced by carcinogen exposure in the trachea, lungs and esophagus in NHP [7,73].

We evaluated 14 spontaneous cases of SCC (13 baboon, 1 spider monkey) in NHP identified over a 20-year period and review 86 additional published cases of spontaneous NHP SCC. NHPs may be a useful animal model for studying SCC.

Materials and Methods

Animals

The baboon colony population averaged approximately 3275 animals (37% male) during the 20-year period. Baboons were occasionally added to the colony for genetic diversity and special projects. Baboons were housed in two 6-acre outdoor corrals, outdoor metal and concrete gang cages, and indoor-outdoor cages. For variable periods of time, baboons were housed inside various buildings individually or in groups for research or other special purposes. The baboons ate a diet of commercial monkey chow supplemented with grains, fruits and vegetables. Water was supplied *ad libitum*. All animal care and procedures were approved by the Southwest Foundation for Biomedical Research Institutional Animal Care and Use Committee. None of the baboons reported in this paper were used in research projects that would have an impact on their likelihood of acquiring SCC.

Pathology

All baboons that died or were euthanized were necropsied and appropriate tissue samples were taken for histologic evaluation. Biopsy specimens taken as an antemortem diagnostic tool were counted with necropsy results from the same animal as one case. All tissues were fixed in 10% neutral buffered formalin, processed conventionally, embedded in paraffin, cut at 5 microns, stained with hematoxylin and eosin, and evaluated by light microscopy by at least one board-certified veterinary pathologist. If deemed necessary, cases were referred to the Armed Forces Institute of Pathology (AFIP) or other individual pathologists for consultation.

Records Review

Pathology records were reviewed for 7578 (4058 female, 3250 male) baboons (*Papio* spp.) necropsied over a 20-year period at the Southwest National Primate Research Center at the Southwest Foundation for Biomedical Research (SFBR). Thirteen cases (11 female, 2 male) of SCC were identified and the original hard-copy medical records, gross necropsy reports, histopathology reports, and histologic slides were obtained. When no hardcopy medical record was available, a computerized version of the medical record was reviewed instead. For each baboon, the following information was obtained: species, age, sex, tumor location, tumor behavior, presenting complaint, and length of treatment. Nine of the 13 cases had been previously reported [13]. Twelve baboons (92.3%) were over 18 years of age and the average age across all 13 baboons was 21.8 years.

Literature review

We performed a literature search for all published cases of spontaneous NHP SCC. Cases of experimentally induced SCC were excluded. We did not include neoplasia that was not specifically listed in a published article. Where discrepancies were seen between reports, the data from the original publication of the case was utilized. Six cases of SCC in macaques from a survey across multiple facilities [43] were excluded as it was not possible to determine if they were duplications of other published cases. Cases were organized by

species and assessed by organ system and location in order of decreasing occurrence and the following information recorded: age at diagnosis, sex, and tumor behavior.

Results

Pathology

The retrospective baboon data is shown in Table 1. The 13 SCC involved the oral cavity ($n = 6$; 46.2%), perineum and vulva ($n = 5$; 38.5%), trachea ($n = 1$; 7.7%), and axillary lymph node ($n = 1$; 7.7%). This is the first known case of spontaneous tracheal SCC reported in a NHP.

All baboon SCC were locally invasive with the exception of the one in the axillary lymph node; a primary site was not identified. Six cases (46.2%) had bone involvement. Five of these involved the oral cavity (4 mandible; 1 maxilla); the other involved the perineum. Five cases (38.5%) had lymph node involvement; these included SCC that originated from the perineum (2), oral cavity (1), trachea (1), and the case where no primary tumor was found; it is unclear whether that tumor arrived at the lymph node by metastasis from an unidentified primary site or if it originated in the lymph node.

SCC of the oral cavity, perineum and vulva presented as proliferative and ulcerative lesions (Figure 1, a–b). The tracheal and axillary lymph node SCC were firm, lobulated masses. All except the vulvar SCC displayed the typical proliferation of neoplastic epithelial cells with the characteristic keratin pearls and intercellular bridges (Figure 1, c–d). Variable numbers of mitotic figures were present and a mixed inflammatory infiltrate was often associated with areas of ulceration or necrosis. The vulvar SCC was a densely cellular unencapsulated mass composed of wide trabeculae of neoplastic cells that infiltrated into the adjacent tissue, had a high mitotic index, and were strongly and diffusely positive with cytokeratin immunohistochemistry.

Clinical presentation

Baboons with oral cavity SCC had irregular soft tissue swelling of the gingiva and buccal mucosa with variable necrosis or ulceration of the oral soft tissues, loose or broken teeth, fracture of the jaw, or abscess formation. Two baboons received treatment. One tumor was surgically excised, but recurred within 5 months. The other baboon received intralesional chemotherapy, but the baboon died during the course of treatment.

Baboons with perineal SCC presented with non-healing, ulcerated and necrotic lesions of the sex skin, vulva, or ischial pads. These cases presented a diagnostic challenge as four of the five were initially diagnosed as trauma and treated. The lesions tended to heal partially, then worsen over time. The average treatment period was 6.1 months and all baboons were eventually euthanized.

Case report

During the course of the records review an additional case of SCC was identified involving the eye of an adult male black spider monkey (*Ateles* spp.). At necropsy, there was extensive local invasion of the periocular tissues, nasal sinus, maxilla, and pituitary. To the best of our knowledge, this is the first reported SCC in a spider monkey.

Literature review

Table 2 lists all NHP SCC in the published literature, and includes the baboon and spider monkey cases reported here. The most frequent NHP species reported with SCC in decreasing order (Table 3) were: macaques ($n = 36$), baboons ($n = 21$), marmosets ($n = 18$),

squirrel monkeys ($n = 11$), tree shrews ($n = 6$), tamarins ($n = 2$), capuchin monkeys ($n = 2$), a black spider monkey ($n = 1$), a sooty mangleby ($n = 1$), a spectacled langur ($n = 1$), and an orangutan ($n = 1$).

The most common reported locations of SCC in all NHP in decreasing order (Table 4) were: oral cavity ($n = 38$; gingiva, tongue, buccal mucosa), integument ($n = 17$; perineum, sex skin, skin), esophagus ($n = 15$), cervix-uterus ($n = 8$), lung ($n = 6$), nasal cavity ($n = 3$), and eye ($n = 2$). SCC was reported once each in the trachea and axillary lymph node. Nine reported cases of SCC involving the soft tissues of the head in marmosets were not identified to a specific location.

The oral cavity was the most common site in all species with more than 2 reported cases, except for the tree shrew, which had no reported oral cavity SCC. Esophageal SCC was mainly seen in macaques and squirrel monkeys, with one case each in a tree shrew and an orangutan.

Baboons developed SCC later in life than macaques ($p < 0.001$); marmosets and tree shrews were diagnosed with SCC at younger ages. SCC in baboons was more common in females than males, while in other species there was generally similar incidence in males and females ($p < 0.05$). All but one case of perineal SCC was seen in female baboons ($p < 0.001$), the exception was a case in a 29-year-old male *Macaca maurus*.

All reported SCC in marmosets involved tissues of the head. SCC of the nasal cavity was only seen in male marmosets ($p < 0.001$). All pulmonary SCC occurred in males; four of the six were in tree shrews, and lung was the most common location for this species. Nasal cavity and pulmonary SCC occurred animals at a much younger age than SCC in other systems.

Metastasis occurred in 23% of NHP (23 of 100), but extensive local invasion was common and often led to the eventual euthanasia of the animal even following surgical excision. Although not statistically significant, there were 9 reports of SCC metastasis in *M. mulatta*, but none in *M. fascicularis*. SCC of the esophagus and oral cavity appeared most likely to metastasize, but also did not reach significance.

Discussion

We reviewed 100 new and reported cases of SCC in NHP and report the first SCC in a spider monkey and the first naturally occurring tracheal SCC in a NHP. The macaque, baboon, and marmoset were the most common species reported; this is likely a reflection of their larger numbers in captivity and use in research rather than an increased species incidence of SCC.

The reason for the male predominance in nasal cavity and pulmonary SCC cases is unknown. The young age of diagnosis for these tumors was likely a result of their presence in species with a shorter lifespan (marmosets, tamarins, and tree shrews).

Baboons were the only species demonstrating a definite sex bias, with females affected overwhelmingly. This may be a result of the high prevalence of perineal neoplasms and a general population bias towards females, particularly among older animals. Although 8 of the 9 reported marmoset cases with known sex were male, the fact that an additional 9 cases were reported without sex information makes any conclusions concerning sex in this species speculative.

Perineal SCC was observed only in females and all but one case were seen in baboons. Several factors may account for this. Increased sunlight exposure is likely a factor: 5 of the 8 reported cases are from SFBR, where the baboons are housed outdoors. Possible contributors in the SFBR colony include sunlight exposure [1,53] trauma to the sex skin [53], and the effects of chronic herpes papio 2 infection [44], or *Histoplasmosis duboisii* infection of the sex skin [12]. SCC in this location often appeared similar to traumatic lesions resulting in delayed diagnosis. Definitive diagnosis by biopsy should be attempted early in the presentation of ulcerative lesions involving the perineum in baboons in order to avoid long ineffective treatment periods.

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References

1. Aiello, SE.; Mays, A., editors. The Merck Veterinary Manual. 8th edition. National Publishing; Philadelphia: 1998. p. 689-691.
2. Altmann D, Kronberger H, Schumann E, Schuppel F, Wolf D, Tunger R. Beitrag zu den Geschwulsten der Primaten. Erkrankungen Zootiere (Berl). 1974;255.
3. Appleby EC, Keymer IF, Hime JM. Three cases of suspected mammary neoplasia in nonhuman primates. J Comp Pathol. 1974; 84:351–364. [PubMed: 4218247]
4. Beniashvili DS. An overview of the world literature on spontaneous tumors in nonhuman primates. J Med Primatol. 1989; 18:423–437. [PubMed: 2693732]
5. Beniashvili, DS. Experimental Tumors in Monkeys. CRC Press; Boca Raton: 1994.
6. Betton GR. Spontaneous neoplasms of the marmoset (*Callithrix jacchus*). Oral and nasopharyngeal squamous cell carcinomas. Vet Pathol. 1983; 21:193–197. [PubMed: 6428027]
7. Bielitzki, JT. Integumentary system. Chapter 9.. In: Bennett; Abee; Henrickson, editors. Nonhuman Primates in Biomedical Research. Diseases. Academic Press; New York: 1998. p. 363-375.
8. Brack M. Spontaneous tumours in tree shrews (*Tupaia belangeri*): Population studies. population studies. J Comp Path. 1998; 118:301–316. [PubMed: 9651807]
9. Brack M, Martin D. Trichoepithelioma in a Barbary ape (*Macaca sylvana*), review of cutaneous tumors in nonhuman primates and case report. J Med Primatol. 1984; 13:159–164. [PubMed: 6502689]
10. Brack M, Schwartz P, Heinrichs T, Schultz M, Fuchs E. Tumors of the respiratory tract observed at the German Primate Center, 1978-1994. J Med Primatol. 1996; 25:424–434. [PubMed: 9210028]
11. Brady, AG.; Morton, DG. Digestive system. Chapter 10.. In: Bennett; Abee; Henrickson, editors. Nonhuman Primates in Biomedical Research. Diseases. Academic Press; New York: 1998. p. 377-414.
12. Butler TM, Hubbard GB. An epizootic of *Histoplasmosis duboisii* (African histoplasmosis) in an American baboon colony. Lab Anim Sci. 1991; 41:407–410. [PubMed: 1666137]
13. Cianciolo RE, Butler SD, Eggers JS, Dick EJ Jr, Leland MM, de la Garza M, Brasky KM, Cummins LB, Hubbard GB. Spontaneous neoplasia in the baboon (*Papio* spp.). J Med Primatol. 2007; 36:61–79. [PubMed: 17493137]
14. Cianciolo RE, Hubbard GB. A review of spontaneous neoplasia in baboons (*Papio* spp.). J Med Primatol. 2005; 34:51–66. [PubMed: 15860111]
15. Cohen DW, Goldman HM. Oral disease in primates. Ann NY Acad Sci. 1969; 85:889–909. [PubMed: 13694359]
16. Crum, CP. The female genital tract. Chapter 24.. In: Cotran; Kumar; Collins, editors. Robbins Pathologic Basis of Disease. WB Saunders; Philadelphia: 1999. p. 1035-1091.

17. DePaoli A, McClure HML. Gastrointestinal neoplasms in nonhuman primates: A review and report of eleven new cases. *Vet Pathol.* 1982; 19(Suppl 7):104–125.
18. DiGiacomo RF, McCann TO. Gynecologic pathology in the *Macaca mulatta*. *Am J Obstet Gynecol.* 1970; 108:538–542. [PubMed: 4990147]
19. Fox, H. Special subjects of pathological interest. Report Laboratory Comparative Pathology; Philadelphia: 1932. p. 16-22.
20. Fox, H. Mortality and matters of pathologic interest. Report of the Penrose Research Laboratory; Philadelphia: 1936. p. 14-19.
21. Fukuda N, Asakura S, Nakagawa S. Two cases of esophageal cancer in monkeys (Abstract). *Jap J Vet Sci.* 1958; 20:303.
22. Grana D, Mareso E, Gomez E. Oral squamous cell carcinoma in capuchin monkeys (*Cebus apella*). Report of two cases. *J Med Primatol.* 1992; 21:384–386. [PubMed: 1307759]
23. Hamerton AE. Report on the deaths occurring in the Society's gardens during the year 1929. *Proc Zool Soc London.* 1930; 1:357.
24. Hertig AT, Macey JJ. Carcinoma in situ of the primate uterus: Comparative observations on the cervix of the crab-eating monkey, *Macaca fascicularis*, the endometrium of the chimpanzee, *Pan troglodytes*, and on similar lesions in the human patient. *Gynecologic Oncol.* 1973; 1:165–183.
25. Hiddleston, WA. Bristol, editor. Veterinary care of Marmosets and Tamarins. Management of Prosimians and New World Primates.; Proceedings of Symposium 8 of the Association of British Wild Animal Keepers. 1984. p. 68-71.
26. Hisaw FL, Hisaw FL Jr. Spontaneous carcinoma of the cervix uteri in a monkey (*Macaca mulatta*). *Cancer.* 1958; 11:810–816. [PubMed: 13561250]
27. Hofmann W, Möller P, Schwaier A, Flügel RM, Zöller L, Darai G. Malignant tumours in *Tupaia* (tree shrew). *J Med Primatol.* 1981; 10:155–163. [PubMed: 6279854]
28. Hubbard GB, Wood DH, Hanton JW. Squamous cell carcinoma with metastasis in a rhesus monkey (*Macaca mulatta*). *Lab Anim Sci.* 1983; 33:469–472. [PubMed: 6645394]
29. Kaspareit J, Friderichs-Gromoll S, Buse E, Korte R, Vogel F. Spontaneous pulmonary neoplasms in cynomolgus monkeys (*Macaca fascicularis*)--A report of two cases. *Exp Toxicol Pathol.* 2001; 53:267–269. [PubMed: 11665850]
30. Kelly AL. Hospital Report. Annual Report of the Executive Secretary 1948-1949 of the Zoological Society of San Diego. *Zoonoz.* 1949; 22:7.
31. Kent SP. Spontaneous and induced malignant neoplasms in monkeys. *Ann NY Acad Sci.* 1960; 85:819–827. [PubMed: 13752561]
32. Klüver H, Brunschwig A. Oral carcinoma in a monkey colony - A report of two additional cases. *Cancer Res.* 1947; 7:627–633.
33. Knightly FA, Lamberski N, Harmon BG, Latimer KS. Squamous cell carcinoma of the perineal skin in two hamadryas baboons (*Papio hamadryas*). *Am Assoc Zoo Vet Annu Conf Proc.* 1996:500–502.
34. Kollias G Jr, Taylor F, Park R. Treatment of squamous cell carcinoma involving the buccal pouch in crab-eating macaque. *J Am Vet Med Assoc.* 1975; 167:664–666. [PubMed: 809400]
35. Kronberger VH, Rittenbach P. Tumours in primates. *Zool Gart (Leipzig).* 1968; 35:205–217.
36. Krotkina NA. A case of spontaneous cancer of the tongue in a monkey. *Vop Onkol.* 1956; 2:748–749.
37. Krylova RI, Kantarija PM. [Spontaneous malignant tumors of the oral cavity in monkeys of Sukhumi nursery.]. *Vopr Onkol.* 1976; 4:99–102. [PubMed: 132010]
38. Langner VC, Garten NF. [Squamous epithelial carcinoma in male red-faced monkey (*Macaca fuscata*).]. *Zool Garten NF.* 1993; 63:1, 59–63.
39. Lapin, BA. The importance of moneys for the study of malignant tumors in man.. In: Bourne, editor. *Nonhuman Primates and Medical Research.* Academic Press; New York: 1973. p. 213-224.
40. Lapin, BA.; Krylova, RI. Verhandlungsbericht des XVIII. Internationalen Symosiums uber die Erkrankungen der Zootiere. Aademie-Verlag; Berlin: 1976. Spontaneous tumors in monkeys of the Sukhumi colony.; p. 249-252.

41. Lapin, BA.; Yakovleva, LA. Comparative Pathology in Monkeys. Thomas; Springfield: 1963. p. 184-188.
42. Lombard LS, Witte EJ. Frequency and types of tumors in mammals and birds of the Philadelphia Zoological Garden. Cancer Res. 1959; 19:127-141. [PubMed: 13629476]
43. Lowenstine, LJ. Neoplasms and proliferative disorders in nonhuman primates.. In: Benirschke, editor. Primates: The Road to Self-Sustaining Populations. Springer-Verlag; New York: 1985. p. 781-814.
44. Martino MA, Hubbard GB, Butler TM, Hilliard JK. Clinical disease associated with Simian Agent 8 infection in the baboon. Lab Anim Sci. 1998; 48:18-22. [PubMed: 9517884]
45. McClure, HM. Neoplasia in rhesus monkeys.. In: Bourne, editor. The Rhesus Monkey. Volume II. Management, Reproduction, and Pathology. Academic Press; New York: 1975. p. 369-398.
46. McClure, MH. Neoplastic diseases in nonhuman primates: Literature review and observations in an autopsy series of 2176 animals.. In: Montali; Migaki, editors. The Comparative Pathology of Zoo Animals. Smithsonian Institution Press; Washington: 1980. p. 549-565.
47. McIntosh GH, Giesecke R, Wilson DF, Goss AN. Spontaneous nasopharyngeal malignancies in the common marmoset. Vet Pathol. 1985; 22:86-88. [PubMed: 3919492]
48. Migaki G, DiGiacomo R, Garner FM. Squamous cell carcinoma of skin in a rhesus monkey (*Macaca mulatta*): Report of a case. Lab Anim Sci. 1971; 21:410-411. [PubMed: 4331305]
49. Montesdeoca D, Roberts J, Donnelly TM. Asymmetry of the face of a squirrel monkey. Lab Anim Sci. 1992; 21:18-21.
50. Morales PR, García A, Stroud FR, Paul KS. Spontaneous cutaneous squamous cell carcinoma in a sooty mangabey (*Cercocebus atys*): A case report. J Am Assoc Lab Anim Sci. 2006; 45:37-40. [PubMed: 16542041]
51. Morin ML, Renquist DM, Allen AM. Squamous cell carcinoma with metastasis in a cynomolgus monkey (*Macaca fascicularis*). Lab Anim Sci. 1980; 30:110-112. [PubMed: 6772874]
52. Morris TH. A further case of squamous cell carcinoma in the oral cavity of a squirrel monkey. J Med Primatol. 1994; 23:317-318. [PubMed: 7710556]
53. Murphy, GF.; Mihm, MC, Jr. The Skin. Chapter 27.. In: Cotran; Kumar; Collins, editors. Robbins Pathologic Basis of Disease. WB Saunders; Philadelphia: 1999. p. 1170-1213.
54. Nakamura S, Sakakibara I, Ono F, Shibata S, Michishita M, Ishii Y, Kobayashi R, Takahashi K, Yoshikawa Y. Squamous cell carcinoma of the oral cavity in an infant cynomolgus monkey. Exp Anim. 2000; 49:225-228. [PubMed: 11109546]
55. Neubauer R, Rabin H, Hopkins S. Characterization of a spontaneous esophageal carcinoma from a rhesus monkey. In Vitro. 1977; 13:174.
56. Ohgaki H, Hasegawa H, Kusama K, Sato S, Kawachi T, Masui M, Tanabe K, Kawasaki I, Hiramatsu H, Saito K. Squamous cell carcinoma found in the cardiac region of the stomach of an aged orangoutang. Gann. 1984; 75:415-417. [PubMed: 6745562]
57. Potkay S. Diseases of Callitrichidae: A review. J Med Primatol. 1992; 21:189-236. [PubMed: 1527793]
58. Rabin H, Neubauer RH, Gonda MA, Nelson-Rees WA, Charman HP, Valerio MG. Spontaneous esophageal carcinoma and epithelial cell line of an adult rhesus monkey. Cancer Res. 1978; 38:331-3314. [PubMed: 620404]
59. Ratcliffe HL. Tumors in captive primates: Report of two cases. Am J Pathol. 1932; 8:117-121. [PubMed: 19969996]
60. Ratcliffe HL. Incidence and nature of tumors in captive wild mammals and birds. Am J Cancer. 1933; 17:116-135.
61. Ratcliffe, HL. Report of the Penrose Research Laboratory. Vol. 7. Philadelphia: Causes of death in the animal collection.; p. 1955
62. Richter CB, Buyukmihci N. Squamous cell of the epidermis in an aged white-lipped tamarin (*Saguinus fuscicollis leucogenys*, Gray). Vet Pathol. 1979; 16:263-265. [PubMed: 108844]
63. Ruch, TC. Diseases of Laboratory Primates. Saunders; Philadelphia: 1959.
64. Sasaki T, Hirokawa M, Usizima H. A spontaneous squamous cell carcinoma of the lower jaw in *Macaca mulatta*. Primates. 1961-1962; 3:82-87.

65. Sasseeville VG, Pauley DR, Spaulding GL, Chalifoux LV, Lee-Parritz D, Simon MA. A spontaneous squamous cell carcinoma of the oral cavity in a squirrel monkey (*Saimiri sciureus*). *J Med Primatol*. 1993; 22:272–275. [PubMed: 7693948]
66. Schlumberger HG. Comparative pathology of oral neoplasms. *Oral Surg Oral Med Oral Pathol*. 1953; 6:1078–1094. [PubMed: 13088006]
67. Schmitz HC, Weishaupt D, Borel N, Padberg B, Bfirki K. The use of ultrasound and computed tomography for the diagnosis of a squamous cell carcinoma of the oesophago-cardial region of the stomach in a rhesus monkey. *Lab Anim*. 2004; 38:92–97. [PubMed: 14979994]
68. Squire, RA.; Goodman, DG.; Valerio, MG.; Fedrickson, T.; Strandberg, JD.; Levitt, MH.; Lingeman, CH.; Harshbarger, JC.; Dawe, CJ. Chapter twelve. Tumors.. In: Benirschke; Garner; Jones, editors. *Pathology of Laboratory Animals*. Vol. II. Springer-Verlag; New York: 1978. p. 1051-1283.
69. Steiner PE, Klüver H, Brunschwig A. Three carcinomas of the tongue in two monkeys. *Cancer Res*. 1942; 2:704–709.
70. Sternberg SS. Carcinoma *in situ* of the cervix in a monkey (*Maccaca mulatta*). *Am J Obstet Gynecol*. 1961; 82:96–98.
71. Sundberg JP. Animal models of papillomavirus research. *Contr Oncol*. 1987; 24:11–38.
72. Sundberg, JP.; Reichmann, ME. Papillomavirus infections.. In: Jones; Mohr; Hunt, editors. *Non-Human Primates II*. Springer-Verlag; New York: 1993. p. 1-8.
73. Weller, RE. Neoplasia/proliferative diseases. Chapter 4.. In: Bennett; Abee; Henrickson, editors. *Nonhuman Primates in Biomedical Research. Diseases*. Academic Press; New York: 1998. p. 208-227.
74. Wood CE, Borgerink H, Register TC, Scott L, Cline JM. Cervical and vaginal epithelial neoplasms in cynomolgus macaques. *Vet Pathol*. 2004; 41:108–115. [PubMed: 15017023]
75. Zhang H-X, Zhang H-L, Zhu D-M, Zhao X-B, Hou B-H. [Esophageal cancer in rhesus monkeys from the Taihang mountain area: A preliminary report.]. *Chin J Oncol*. 1992; 14:411–413.
76. Zuckerman S. A rhesus macaque (*Macaca mulatta*) with carcinoma of the mouth. *Proc Zool Soc (Lond)*. 1930; 1:59–61.

Figure 1.

Gross and histological presentation of squamous cell carcinoma in the baboon. A, Oral cavity. Note the expansile and ulcerative mass involving the rostral mandible and the loss of teeth, B, Perineum. The baboon is laying on it's left side with extensive ulceration and necrosis of the perineum. C, Trachea. Note: The nests and packets of neoplastic epithelial cells and formation of keratin pearls. H&E, Bar = 500 μ m. D, Bone. Note the nests and packets of neoplastic epithelial cells and formation of keratin pearls admixed with bone trabeculae and loose fibrous connective tissue. H&E, Bar = 200 μ m.

Table 1

SCC in thirteen SFBR baboons.^a

Tumor Location	Age (yr)	Sex	Tumor Behavior	Presenting Complaint	Treatment Period (from presentation to death)
Oral, Gingiva and mandible	20.2	M	Local invasion of bone	Mandibular cavitation	None; biopsy diagnosis; euthanized
Oral, Gingiva and mandible	26	M	Local invasion of bone	Gingival mass	5 months; biopsy diagnosis; surgical excision attempted; recurrence of tumor; euthanized
Oral, Gingiva and maxilla	3	F	Local invasion of bone and medullary cavity with tumor in blood vessels	Maxillary swelling	3 months; antibiotic therapy unsuccessful; biopsy diagnosis; intralesional chemotherapy attempted; died during treatment
Oral, Buccal mucosa	19.2	F	Local invasion (mucosa and subcutaneous tissue) with extension or metastasis to regional lymph node	Eroded mass on left cheek	None; biopsy diagnosis; lived 3 months post-biopsy to raise young, then euthanized
Oral, Skin and mandible ^b	19.3	F	Local invasion of bone with pathologic fracture	Mandibular fracture	None; euthanized on presentation
Oral, Gingiva, buccal pouch and mandible	20.3 ^c	F	Local invasion of bone	Mandibular fracture	None; euthanized on presentation
Perineum, Sex skin and haired skin	20.3	F	Local invasion of bone and medullary cavity with extension or metastasis to regional lymph node	Skin sloughing with bone necrosis	3.5 months; topical, antibiotic and antifungal therapy unsuccessful; euthanized
Perineum, Sex skin	22.7	F	Local invasion (sex skin and subcutaneous tissue)	Sex skin laceration	6 months; antibiotic therapy unsuccessful; biopsy diagnosis; euthanized
Perineum, Sex skin ^b	24.7	F	Local invasion (skin and subcutaneous tissues)	Sex skin laceration	10 months; topical and antibiotic therapy unsuccessful; biopsy diagnosis; euthanized
Perineum, Sex skin ^b	25.5	F	Local invasion (skin and subcutaneous tissues)	Laceration / Sloughing of sex skin	5 months; antibiotic therapy unsuccessful; euthanized
Perineum, Vulva	31.7	F	Local invasion with extension and lymph node metastasis near cervix with obstruction of rectum and partial ureteral obstruction leading to hydronephrosis	Vulvar and anal necrosis	None; euthanized on presentation
Trachea ^b	18	F	Local invasion of trachea with extension or metastasis to regional lymph node	Difficulty breathing	None; exploratory surgery performed; euthanized postoperatively
Axillary lymph node	33	F	No primary tumor identified	Old age changes; tumor incidental finding at necropsy	None

^a All cases except those noted were previously published [13].

^b New case.

^c Previously reported as 19 years old

Table 2

Reported squamous cell carcinoma in nonhuman primates.

Species	Organ System	Location	Age	Sex	Metastasis	Tumor Behavior	References
<i>Macaca mulatta</i>	Digestive	Esophagus	Adult	Male	Yes	Local invasion. Metastasis to renal lymph nodes and ribs.	4,55
<i>Macaca mulatta</i>	Digestive	Esophagus	>11 years	Male	Yes	Local invasion. Metastasis to lymph nodes.	4,17,58
<i>Macaca mulatta</i>	Digestive	Esophagus	11 years	Female			75
<i>Macaca mulatta</i>	Digestive	Esophagus	7 years	Male	Yes	Metastasis to mediastinum and regional lymph nodes.	75
<i>Macaca mulatta</i>	Digestive	Gastric cardia	5 years	Female	Yes	Local invasion. Metastasis to lung.	67
<i>Macaca mulatta</i>	Digestive	Oral cavity	10 years	Male	Not reported.	Local invasion.	4,5,17,37,40
<i>Macaca mulatta</i>	Digestive	Oral cavity	9 years	Female	Yes	Local invasion. Metastasis to regional lymph nodes.	6,17,45,48,64,68
<i>Macaca mulatta</i>	Digestive	Oral cavity	Adult	Male	Not reported.	Local invasion.	5,6,15,17,23,31,45,48,64,66,68,76
<i>Macaca mulatta</i>	Digestive	Tongue	14 years	Male	Yes	Local invasion. Metastasis to cervical lymph nodes.	5,6,17,31,32,48,63,64,68
<i>Macaca mulatta</i>	Digestive	Tongue	25 years	Male	Not reported.	Not reported.	6,15,17,31,36,48,63,64,68
<i>Macaca mulatta</i>	Digestive	Tongue	16 years	Male	Not reported.	Two tumors. Local invasion.	5,6,15,17,31,32,48,63,64,66,68,69
<i>Macaca mulatta</i>	Integumentary	Skin, prepuce, penis	21 years	Male	Yes	Metastasis to regional lymph nodes and lung.	4,28
<i>Macaca mulatta</i>	Integumentary	Skin, penis	Adult	Male			5,10,43,46
<i>Macaca mulatta</i>	Integumentary	Skin, mammary area	Adult	Female	Yes	Metastasis to skin, axillary lymph node, colon.	3,5,6,7,9,43,45,46,48,68
<i>Macaca mulatta</i>	Reproductive	Cervix		Female	Not reported.	Not reported.	18,24
<i>Macaca mulatta</i>	Reproductive	Cervix	Adult	Female	Not reported.	Not reported.	24,48,70
<i>Macaca mulatta</i>	Reproductive	Cervix uteri	Not reported.	Female	Yes	Metastasis to urinary bladder, lymph nodes, and lungs. Hydronephrosis.	5,6,24,26,31,45,48
<i>Macaca mulatta</i>	Special senses	Eye	38 years	Male	Not reported.	Local invasion.	43
<i>Macaca fascicularis</i>	Reproductive	Cervix	Adult	Female	Not reported.	Not reported.	24
<i>Macaca fascicularis</i>	Reproductive	Cervix	22 years	Female	Not reported.	Not reported.	74

Species	Organ System	Location	Age	Sex	Metastasis	Tumor Behavior	References
<i>Macaca fascicularis</i>	Reproductive	Cervix	23 years	Female	Not reported.	Not reported.	74
<i>Macaca fascicularis</i>	Reproductive	Vulva	12 years	Female	Not reported.	Not reported.	4,5,51
<i>Macaca fascicularis</i>	Digestive	Buccal mucosa	14 years	Female	Not reported.	Surgical removal, then recurrence. Second surgical removal and radiation treatment.	4,17,34,43,46
<i>Macaca fascicularis</i>	Digestive	Oral cavity	1 year	Male	Not reported.	Not reported.	54
<i>Macaca fascicularis</i>	Respiratory	Lung	7 years	Male	Not reported.	Not reported.	29
<i>Macaca fuscata</i>	Digestive	Esophagus	5 years	Male	Not reported.	Not reported.	17,21
<i>Macaca fuscata</i>	Digestive	Gastroesophageal junction	>16 years	Male	Yes	Local invasion. Metastasis to splenic lymph nodes.	6,17,19,31,42,59,60,68
<i>Macaca fuscata</i>	Digestive	Oral cavity	6 years	Male	Not reported.	Not reported.	38
<i>Macaca arctoides</i>	Digestive	Oral cavity	15 years	Male	Not reported.	Local invasion.	4,5,37,40
<i>Macaca arctoides</i>	Digestive	Oral cavity	16 years	Not reported.	Yes	Local invasion. Metastasis to mandibular and axillary lymph nodes.	4,5,17,37,40
<i>Macaca cyclopsis</i>	Digestive	Esophagus	Adult	Female	Not reported.	Not reported.	17,21
<i>Macaca irus</i>	Digestive	Tongue	12 years	Male	Yes	Local invasion. Metastasis to submaxillary lymph node.	5,6,15,17,31,32,48,63,64,66,68,69
<i>Macaca mauns</i>	Integumentary	Skin, rump	29 years	Male	Not reported.	Not reported.	5,6,31,42,43,61,68
<i>Macaca sinica</i>	Reproductive	Cervix	Not reported.	Female	Not reported.	Not reported.	5,20,31,68
<i>Macaca speciosa</i>	Digestive	Esophagus	18 years	Male	Not reported.	Local invasion.	17,35,68
<i>Macaque</i>	Digestive	Gastroesophageal junction	12 years	Female	Not reported.	Local invasion.	2
<i>Papio hamadryas</i>	Integumentary	Sex skin	19 years	Female	Not reported.	Local invasion.	5,14,41,46,68
<i>Papio</i> spp.	Integumentary	Sex skin	23 years	Female	Not reported.	Local invasion, sex skin and subcutaneous tissue)	13
<i>Papio</i> spp.	Integumentary	Sex skin	25 years	Female	Not reported.	Local invasion, sex skin and subcutaneous tissue)	
<i>Papio</i> spp.	Integumentary	Sex skin	25 years	Female	Not reported.	Local invasion, sex skin and subcutaneous tissue)	
<i>Papio</i> spp.	Integumentary	Sex skin and haired skin, right hip	20 years	Female	Yes	Local invasion of bone. Spread to regional lymph nodes.	13
<i>Papio hamadryas</i>	Integumentary	Perineum	Aged	Female	Not reported.	Local Invasion.	14,33

Species	Organ System	Location	Age	Sex	Metastasis	Tumor Behavior	References
<i>Papio hamadryas</i>	Integumentary	Perineum	Aged	Female	Not reported.	Local Invasion.	14,33
<i>Papio</i> spp.	Integumentary	Perineum	Adult	Female	Not reported.	Not reported.	43
<i>Papio</i> spp.	Integumentary	Vulva	32 years	Female	Not reported.	Local invasion with extension or metastasis near cervix with obstruction of rectum and partial ureteral obstruction leading to hydronephrosis.	13
Long Armed Baboon	Integumentary	Skin, right breast	Not reported.	Female	Not reported.	Squamous cell epithelioma.	3,14,30,42,68
Baboon	Digestive	Gingiva	Not reported.	Not reported.	Not reported.	Not reported.	14,15,68
<i>Papio</i> spp.	Digestive	Gingiva and mandible	20 years	Male	Not reported.	Local invasion of bone.	13
<i>Papio</i> spp.	Digestive	Gingiva and mandible	26 years	Male	Not reported.	Local invasion of bone.	13
<i>Papio</i> spp.	Digestive	Gingiva and mandible	19 years	Female	Not reported.	Local invasion of bone with pathologic fracture.	
<i>Papio</i> spp.	Digestive	Gingiva and maxilla	3 years	Female	Not reported.	Local invasion of bone.	13
<i>Papio</i> spp.	Digestive	Gingiva, buccal pouch and mandible	20 years	Female	Not reported.	Local invasion of bone with pathologic fracture	13
<i>Papio</i> spp.	Digestive	Buccal mucosa	19 years	Female	Yes	Local invasion. Metastasis to regional lymph nodes.	13
<i>Papio</i> spp.	Digestive	Oral cavity	11 years	Male	Not reported.	Not reported.	43
	Digestive	Oral cavity	Not reported.	Not reported.	Yes	Local Invasion. Metastasis to regional lymph nodes.	6,14,15,17,66,68
<i>Papio</i> spp.	Respiratory	Trachea	18 years	Female	Yes	Local invasion. Metastasis to regional lymph nodes.	
<i>Papio</i> spp.	Lymphatic	Axillary lymph node	33 years	Female	Not reported.	No primary tumor identified.	13
<i>Callithrix jacchus</i>	Digestive	Oral cavity	4 years	Female	Not reported.	Local invasion.	4,5,6
<i>Callithrix jacchus</i>	Digestive	Oral cavity	5 years	Male	Not reported.	Local invasion to nasal turbinates.	4,5,6
<i>Callithrix jacchus</i>	Digestive	Oral cavity	5 years	Male	Not reported.	Local invasion to nasal cavity and retrobulbar space.	4,5,6
<i>Callithrix jacchus</i>	Digestive	Soft palate	4 years	Male	Not reported.	Local invasion to retroorbital space and optic nerve.	4,5,6
<i>Callithrix jacchus</i>	Digestive	Soft palate	6 years	Male	Yes	Local invasion to pharynx, retrobulbar space. Metastasis to lung.	4,5,6

Species	Organ System	Location	Age	Sex	Metastasis	Tumor Behavior	References
<i>Callithrix jacchus</i>	Digestive	Maxillary palate	> 8 years	Male	Not reported.	Not reported.	4,5,6
<i>Callithrix jacchus</i>	Respiratory	Nasal cavity	4 years	Male	Not reported.	Not reported.	47
<i>Callithrix jacchus</i>	Respiratory	Nasopharynx	> 10 years	Male	Yes	Local invasion through the bones of the cranium. Metastasis to lung.	4,5,6
<i>Callithrix jacchus</i>	Respiratory	Nasopharynx	6 years	Male	Not reported.	Local invasion through the bones of the cranium.	4,5,6
Marmoset	Not reported.	Soft tissues of head	Not reported.	Not reported.	Not reported.	Not reported.	25,57
Marmoset	Not reported.	Soft tissues of head	Not reported.	Not reported.	Not reported.	Not reported.	25,57
Marmoset	Not reported.	Soft tissues of head	Not reported.	Not reported.	Not reported.	Not reported.	25,57
Marmoset	Not reported.	Soft tissues of head	Not reported.	Not reported.	Not reported.	Not reported.	25,57
Marmoset	Not reported.	Soft tissues of head	Not reported.	Not reported.	Not reported.	Not reported.	25,57
Marmoset	Not reported.	Soft tissues of head	Not reported.	Not reported.	Not reported.	Not reported.	25,57
Marmoset	Not reported.	Soft tissues of head	Not reported.	Not reported.	Not reported.	Not reported.	25,57
Marmoset	Not reported.	Soft tissues of head	Not reported.	Not reported.	Not reported.	Not reported.	25,57
Marmoset	Not reported.	Soft tissues of head	Not reported.	Not reported.	Not reported.	Not reported.	25,57
Marmoset	Not reported.	Soft tissues of head	Not reported.	Not reported.	Not reported.	Not reported.	25,57
<i>Saimiri sciurea</i>	Digestive	Oral cavity	8 years	Female	Not reported.	Not reported.	5,15,17,31,32,48,63,64,68
<i>Saimiri sciurea</i>	Digestive	Oral cavity	Adult	Male	Not reported.	Local invasion.	5,40
<i>Saimiri sciurea</i>	Digestive	Oral cavity	Adult	Male	Not reported.	Local invasion.	5,40
<i>Saimiri sciurea</i>	Digestive	Oral cavity	Adult	Male	Yes	Local invasion. Metastasis to lymph nodes.	11,49,65
<i>Saimiri sciurea</i>	Digestive	Oral cavity	> 13 years	Male	Not reported.	Not reported.	52
<i>Saimiri sciurea</i>	Digestive	Oral cavity	> 20 years	Female	Yes	Local invasion of bone. Metastasis to regional lymph nodes.	52,65
<i>Saimiri sciurea</i>	Digestive	Oral cavity	Adult	Male	Not reported.	Not reported.	17,39,40
<i>Saimiri sciurea</i>	Digestive	Oral cavity	Adult	Female	Not reported.	Not reported.	17,39,40
<i>Saimiri sciurea</i>	Digestive	Esophagus	Adult	Female	Not reported.	Local invasion.	40
<i>Saimiri sciurea</i>	Digestive	Esophagus	Adult	Female	Not reported.	Local invasion.	5,40
<i>Saimiri sciurea</i>	Digestive	Esophagus	Adult	Female	Not reported.	Local invasion.	5,40
<i>Tupaia belangeri</i>	Respiratory	Lung	8 months	Male	Not reported.	Not reported.	10
<i>Tupaia belangeri</i>	Respiratory	Lung	8 years	Male	Not reported.	Not reported.	10

Species	Organ System	Location	Age	Sex	Metastasis	Tumor Behavior	References
<i>Tupaia belangeri</i>	Respiratory	Lung	1 year	Male	Yes	Metastasis to lung (multiple nodules).	8
<i>Tupaia belangeri</i>	Respiratory	Lung	1 year	Male	Not reported.	Not reported.	8
<i>Tupaia belangeri</i>	Digestive	Esophagus	3 years	Female	Yes	Metastasis to spleen.	8
<i>Tupaia</i>	Reproductive	Corpus uteri	10 years	Female	Not reported.	Not reported.	4,5,27
<i>Cebus apella</i>	Digestive	Oral cavity	12 years	Male	Not reported.	Local invasion of bone.	22
<i>Cebus apella</i>	Digestive	Oral cavity	14 years	Male	Not reported.	Local invasion of bone.	22
<i>Saguinus fuscicollis leucogenys</i>	Integumentary	Skin	> 15 years	Female	Not reported.	Not reported.	5,7,9,57,62
<i>Saguinus fuscicollis</i>	Respiratory	Lung	Not reported.	Male	Not reported.	Not reported.	10,29
<i>Ateles</i> spp.	Special senses	Eye	Adult	Male	Not reported.	Local invasion of eye, periorbital and nasal tissues, bone, and pituitary.	
<i>Pongo pygmaeus</i>	Digestive	Gastric cardia	28 years	Male	Yes	Local invasion. Metastasis to lymph nodes, liver, spleen, and lung.	4,43,56
<i>Cercocebus atys</i>	Integumentary	Skin, dorsolateral cervical area	Adult		Not reported.	Not reported.	50
<i>Presbytis obscurus</i>	Digestive	Oral cavity	2.5 yrs	Male	Not reported.	Not reported.	43

Table 3

NHP species most commonly reported with SCC.

Species (n) = 94	Macaque 36	Baboon 21	Marmoset 18	Squirrel monkey 11	Tree shrew 6	P
Age: n=61, age	26, 14.4 ± 1.6 ^a	15, 20.8 ± 1.9	9, 5.7 ± 0.7 ^{a,b}	3, 13.6 ± 3.5	6, 4.0 ± 1.6 ^{a,b}	<0.001
Sex (M/F) N=80	20/15 ^a	3/16	8/1 ^a	5/6	4/2 ^a	<0.05
Location (#) N=85	36	21	9	11	6	<0.001
Oral cavity (#)	12	9	6	8 ^b	0 ^{a,c}	<0.05
Integumentary (#)	5 ^a	10	0 ^a	0 ^a	0 ^a	<0.05
Esophagus (#)	10 ^a	0	0	3 ^a	1	0.509
Cervix and Uterus (#)	7	0	0	0	1	0.744
Lung (#)	1	0	0	0	4 ^a	0.890
Eye (#)	1	0	0	0	0	
Trachea (#)	0	1	0	0	0	
Lymph node (#)	0	1	0	0	0	
Nasal cavity (#)	0	0	3 ^{a,b}	0	0	0.726
Metastasis (#) N=94	12	4	2	2	2	0.670

^a vs. Baboon^b vs. Macaque^c vs. Marmoset

Table 4

Most common SCC locations in NHP.

Location	Age in yr (<i>n</i> = 61)	Sex (<i>n</i> = 83) M/F	Metastasis (%)
Oral cavity (<i>n</i> = 38)	30, 11.9 ± 1.2	35, 25/10	9 (25)
Integument (<i>n</i> = 17)	10, 22.1 ± 1.9 ^a	16, 3/13	3 (17.6)
Esophagus (<i>n</i> = 15)	10, 11.6 ± 2.3 ^b	15, 7/8 ^c	7 (46.6)
Cervix, Uterus (<i>n</i> = 8)	3, 18.3 ± 4.1	8, 0/8 ^{a,c}	1 (12.5)
Lung (<i>n</i> = 6)	5, 3.6 ± 1.6 ^{a,b,c,d}	6, 6/0 ^{b,c,d}	1 (16.6)
Nasal cavity (<i>n</i> = 3)	3, 6.6 ± 1.7 ^{b,d}	3, 3/0 ^{b,d}	1 (33.3)

^a *p* < 0.001 vs. Oral cavity^b *p* < 0.001 vs. Integumentary^c *p* < 0.001 vs. Esophagus^d *p* < 0.001 vs. Cervix, Uterus