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Neoplasia in the Chimpanzee (*Pan* spp.)

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Abstract

Background—Chimpanzees have over 98% genomic sequence homology with humans and may have a similar host response to malignancy. There is minimal information concerning cancer in the chimpanzee and such information would be valuable to individuals caring for and using them for research.

Methods—Spontaneous neoplasia that was documented in two chimpanzee colonies and in the literature were evaluated statistically.

Results—In all, 105 spontaneous and 12 experimental neoplasms were diagnosed. Seventy-four spontaneous tumors occurred in females, 24 in males, and 7 in animals of undetermined sex. Of the spontaneous tumors 89 were benign, 14 were malignant, and 2 were undetermined.

Neoplasia was most common in the urogenital system in females.

Conclusions—Neoplasia is not uncommon in the chimpanzee, is generally benign, and occurs primarily in the urogenital system in females.

Keywords

Ape; nonhuman primate; cancer; tumor; disease; leiomyoma

INTRODUCTION

Chimpanzees have over 98% genomic sequence homology with humans and may have a similar host response to malignancy [25]. Neoplasia was once considered to be uncommon in nonhuman primates and especially in chimpanzees, but now it is increasingly common as nonhuman primate colony populations age [8,10,17,19,20,22]. The prevalence and characteristics of neoplasia in chimpanzees are valuable for people maintaining colonies and using chimpanzees for research. While much has been written about diseases of chimpanzees, little or no comprehensive information about neoplasia in this valuable laboratory animal has been collected [7,13,29,30,33,34]. Several publications in the nonhuman primate literature contain information about neoplasia in chimpanzees [4,5,10,11,15,17,19-23,24,31,36,38,42], however with the exception of one involving 12

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neoplasms [17] most consist of case reports from few animals and often involve only a single system. This paper provides a comprehensive evaluation of chimpanzee neoplasia by reporting 53 documented chimpanzee neoplasms from two major chimpanzee facilities and including a review of all reported neoplasia in the chimpanzee.

METHODS

Case Reports

We report on all neoplasia documented at two major chimpanzee facilities from inception through April of 2008, the Southwest National Primate Research Center at the Southwest Foundation for Biomedical Research (SNPRC) and the Yerkes National Primate Research Center at Emory University (YNPRC). Neoplasms were identified and confirmed using the pathology records at both primate centers.

Literature Search

We also performed a literature search for all published cases of chimpanzee neoplasia, both captive and wild, spontaneous and experimental. Cases were assessed by system and location in order of decreasing occurrence (Table 1). We also include a list of tumor diagnoses, malignancy, age of the host at diagnosis of the tumor, and sex of the host. We did not include neoplasia that was not specifically listed in a published article. A prime example of this would be a report on papillomas in which individual cases were representative of colony outbreaks. Only the case(s) described in the article would be included in the table.

Neoplasia Classification

If a tumor had multiple sites in one organ, it was counted as one neoplasm. If the same nonmetastatic primary tumor was found in both paired organs in the same chimpanzee it was considered as a separate tumor in each paired organ. An example of this would be the fibrothecomas found in both ovaries of one chimpanzee. Pertinent comments and references are provided as necessary; the neoplasms without references were from the SNPRC or YNPRC and not previously reported in the literature. All papillomas were placed in the integumentary system. The alimentary system included the salivary glands, exocrine pancreas, and liver. Endocrine tumors of the pituitary, adrenal, thyroids, kidney, and endocrine pancreas were included with the endocrine system. Two neoplasms, a lipoma and an endothelioma, could not be placed in any system with confidence but were placed last in the most likely system of occurrence.

It was extremely difficult to determine whether some published cases of neoplasia were reported more than once because data such as age, sex, location, and tumor type were often missing, especially in older publications. Additionally, many of the reviews included tumors that may have been included in a previous report. If there was any question that the tumor was a true neoplasm or that it was duplicated in the literature, it was excluded.

Statistical Analysis

Twelve experimental neoplasms were included for completeness but were excluded from the statistical evaluation of the spontaneous cases. Also excluded from statistical evaluation were two spontaneous tumors, an endothelioma and a brain tumor, for which the information was inadequate for proper statistical evaluation. Neoplasms were evaluated by organ system and compared for age at diagnosis, sex, and malignancy. Four spontaneous neoplasms from systems containing less than 3 neoplasms with adequate information (musculoskeletal and hematopoietic) were excluded from this analysis. All spontaneous neoplasms were compared for age at diagnosis and sex based on malignancy.

Data are presented as mean ± SEM. Due to the abnormal distribution of the data, Mann-Whitney and Kruskal-wallis test were used for comparisons of numeric variables between two and more than two groups, respectively, and Fisher's exact test to compare qualitative variables.

RESULTS

Table 1 lists all tumors of chimpanzees in the published literature as well as all tumors that were documented at the YNPRC and the SNPRC through April of 2008. Tables 2 and 3 provide all relevant statistics. In all, 105 spontaneous and 12 experimental neoplasms were diagnosed. Seventy-four spontaneous tumors occurred in females, 24 in males and 7 in chimpanzees of undetermined sex. Two chimpanzees had three tumors and four had two each. Of the spontaneous tumors, 89 were benign, 14 malignant, and 2 were undetermined. Spontaneous neoplasia was diagnosed in an ape less than two months of age. In females, neoplasia was most common in the urogenital system followed in decreasing frequency by the integumentary, endocrine, alimentary, respiratory, and musculoskeletal, and cardiovascular systems. The most common tumor was the leiomyoma of the uterus, cervix, and vagina. In males, neoplasia was most common in the alimentary system followed in decreasing occurrence by the endocrine, cardiovascular, integumentary, respiratory, hematopoietic, and urogenital systems. The most common tumor was the hemangioma. Respiratory neoplasms were identified in animals at a younger age ($p<0.05$) and alimentary neoplasms were more likely to be malignant ($p<0.05$) when compared to other systems. Overall, malignant neoplasms were more common in males ($p=.038$) and were diagnosed in animals at younger ages ($p<0.05$).

DISCUSSION

This paper statistically evaluated 103 of the 105 cases of spontaneous neoplasia in the chimpanzee. Previous reports of chimpanzee neoplasia lacked adequate numbers to evaluate organ system predilection and incidence by age or sex. While it would have been interesting to compare types of neoplasms seen between the two facilities, there were inadequate numbers for meaningful analysis. We found that neoplasia is common in chimpanzees. It is also clear that while most tumors were benign, malignancies do occur.

Neoplasms in the gastrointestinal system were much more likely to be malignant than those found in other organ systems. The incidence of neoplasia was much higher in females than males due to the high incidence of neoplasia in the female urogenital system. The most common neoplasm in females was the leiomyoma of the uterus and associated structures. This high incidence of leiomyomas, generally in older female animals, probably explains the finding that malignant neoplasms were more common in males and younger chimpanzees. Tumors were found in all systems, however, there was only one poorly documented tumor of the central nervous system, in the brain. It was interesting that the systems most commonly affected with neoplasia aside from the urogenital system were quite different for males and females.

While tumors tend to occur in older animals, one tumor was found in a 52-day-old chimpanzee, so clinicians should be aware of the possibility of neoplasia in young individuals. Generally, neoplasms in the respiratory system occurred in younger chimpanzees than those in other systems.

Chimpanzee numbers, even in large colony populations, pale in comparison to the human population and a direct comparison between the two species of the incidence of neoplasia is not possible. It is also apparent from our review that many tumors occurring in our colonies

would have gone unreported and it is likely that this is not uncommon in other large populations.

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Table 1

Neoplasia in the chimpanzee.

Case #	Location	Diagnosis	Sex	Age (Years) at Diagnosis	Malignant or Benign	Comments[a]	Reference
Urogenital System							
1	Uterus	Leiomyoma	F	31	B		
2	Uterus	Leiomyoma	F	44	B		
3	Uterus	Leiomyoma	F	40	B		
4	Uterus	Leiomyoma	F	40	B		
5	Uterus	Leiomyoma	F	31	B		
6	Uterus	Leiomyoma	F	45	B		
7	Uterus	Leiomyoma	F	32	B		
8	Uterus	Leiomyoma	F	41	B		
9	Uterus	Leiomyoma	F	36	B		
10	Uterus	Leiomyoma	F	37	B		
11	Uterus	Leiomyoma	F	29	B		
12	Uterus	Leiomyoma	F	38	B		
13	Uterus	Leiomyoma	F	41	B		
14	Uterus	Leiomyoma	F	28	B		
15	Uterus	Leiomyoma	F	42	B		
16	Uterus	Leiomyoma	F	44	B		
17	Uterus	Leiomyoma	F	55	B		
18	Uterus	Leiomyoma	F	19	B		43
19	Uterus	Leiomyoma	F	23	B		36
20	Uterus	Leiomyoma	F	25	B		41
21	Uterus	Leiomyoma	F	40	B		
22	Uterus	Leiomyoma	F	26	B		
23	Uterus	Leiomyoma	F	39	B		
24	Uterus	Leiomyoma	F	47	B		
25[b]	Uterus	Leiomyoma	F	42	B	Experimental HBV infection	
26	Uterus	Leiomyoma	F	22	B		37

Case #	Location	Diagnosis	Sex	Age (Years) at Diagnosis	Malignant or Benign	Comments[a]	Reference
27	Cervix, vagina	Leiomyoma	F	45	B		
28	Oviduct	Leiomyoma	F	31	B		
29	Kidney	Carcinoma	F	17	M		12
30	Unk	Leiomyoma	F	44	B		39
31	Unk	Leiomyoma	F	44	B		39
32	Unk	Leiomyoma	F	44	B		39
33	Unk	Leiomyoma	F	47	B		39
34	Unk	Leiomyoma	F	23	B		
35	Vagina	Leiomyoma	F	31	B		
36	Vagina	Leiomyoma	F	26	B		
37	Vagina	Angiofibroma	F	47	B		
38	Uterus	Adenocarcinoma *in situ*, endothelium	F	23	M	Adenomatous hyperplasia of endometrium	17
39	Uterus	Carcinoma	F	Unk[b,c]	M		16
40	Uterus	Endometrial stromal	F	25	B		41
41	Uterus	Partial hydatid mole	F	30	B	Mole in placenta of stillborn	9
42	Uterus	Polyp	F	40	B		4
43	Ovary	Fibrothecoma	F	38	B		11
44	Ovary	Fibrothecoma	F	48	B		11
45	Ovary	Fibrothecoma	F	48	B		11
46	Ovary	Granulosa cell tumor	F	31	B		
47	Ovary	Granulosa cell tumor	F	32	B		
48	Ovary	Teratoma	F	22	B		
49	Ovary	Brenner tumor, right ovary	F	32	B		
50	Ovary	Sertoli-Leydig cell tumor	F	38	B		11
Integumentary System							
51	Skin	Papilloma	F	4	B		35

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Case #	Location	Diagnosis	Sex	Age (Years) at Diagnosis	Malignant or Benign	Comments[a]	Reference
52	Skin	Papilloma	F	1	B		
53	Skin	Papilloma	F	25	B		
54	Skin	Papilloma	F	27	B		
55	Skin	Papilloma	Unk[b]	Unk[b]	B		17
56	Skin	Papilloma	Unk[b]	Unk[b]	B	*Pan paniscus*	40
57	Unk	Papilloma	M	7	B		10
58	Unk	Papilloma	M	Adult	B		10
59	Unk	Papilloma	M	Unk[b]	B		10
60	Unk	Papilloma	Unk[b]	Unk[b]	B		10
61	Subcutis	Lipoma	F	29	B		17
62	Subcutis	Lipoma	F	31	B		
63	Subcutis	Lipoma	F	35	B		
64	Subcutis	Lipoma	F	44	B		17
65	Subcutis	Lipoma	F	28	B		
66	Unk	Lipoma	Unk[b]	Unk[b]	B		17
67	Unk	Basosquamous cell carcinoma	F	39	M		
68	Subcutis	Nevus lipomatosus cutaneous superficialis	M	32	B		16
69[b]	Subcutis	Osteosarcoma	Unk	Unk	M	Transplant of human osteosarcoma nonproducer cells infected with baboon endogenous virus	28
Endocrine System							
70	Pituitary	Adenoma	F	44	B		
71	Pituitary	Adenoma	F	32	B		
72	Pituitary	Adenoma	M	46	B		
73	Pituitary	Adenoma	F	22	B		
74	Adrenal	Cortical adenoma	M	34	B		
75	Adrenal	Cortical adenoma	F	8	B		17

Case #	Location	Diagnosis	Sex	Age (Years) at Diagnosis	Malignant or Benign	Comments[a]	Reference
76	Adrenal	Neurofibroma	M	28	B		
77	Thyroid	Follicular cell Adenoma	F	31	B		
78	Thyroid	Follicular cell adenoma	M	28	B		
79	Thyroid	Thyroid carcinoma	M	34	M		
80	Pancreas	Islet cell adenoma	M	16	B		17
81	Pancreas	Islet cell (adenomatosis)	F	47	B		17
82	Kidney	Ectopic adrenalcortical carcinoma	F	47	B		17
Alimentary System							
83	Liver	Hepatocellular carcinoma	M	16	M		
84	Liver	Hepatocellular carcinoma	M	34	M		
85	Liver	Hepatocellular carcinoma	F	28	B		
86	Liver	Hepatocellular carcinoma	M	16	M		27
87[b]	Liver	Hepatocellular carcinoma	F	12	M	Chronic *Schistosoma mansoni* infection; HBV/HCV	1
88[b]	Liver	Hepatocellular carcinoma	M	14	M	Experimental infection: NANBH human plasma (w/chronic HCV)	24
89[b]	Liver	Hepatocellular carcinoma	M	7	M	Experimental HBV infection; delta hepatitis; no NANBH exposure	24
90[b]	Liver	Hepatocellular carcinoma	M	28	M	Experimental HBV	
91[b]	Liver	Carcinoma, poorly differentiated	F	42	M	Experimental HBV infection	
92[b]	Liver	Hepatocellular adenoma	M	17	B	Experimental infection: NANBH human plasma; HBV/HCV +; tumor diagnosis questionable -	24

Case #	Location	Diagnosis	Sex	Age (Years) at Diagnosis	Malignant or Benign	Comments[a]	Reference
						described as resembling hepatocellular carcinoma	
93[b]	Liver	Myelolipoma	M	21	B	Experimental HCV/HIV infection	27
94	Stomach	Gastrointestinal stromal tumor	M	22	B		32
95	Colon	Gastrointestinal stromal tumor	M	33	B		
96[b]	Rectum	Gastrointestinal stromal tumor	F	42	B	Experimental HBV infection	
97	Gall bladder	Adenoma	F	37	B		39
98	Duodenum	Adenomatosis benign glandular tumor of the Brunner's glands	F	44	B		17
99	Jejunum	Polyposis	M	40	B		10
100	Rectum	Leiomyosarcoma	F	26	M		
101	Parotid salivary gland	Adenocarcinoma	M	40	M		
Cardiovascular System							
102	Kidney	Hemangioma	M	31	B		
103	Kidney	Hemangioma	M	33	B		
104	Spleen	Hemangioma	M	29	B		
105	Subcutis	Hemangioma	F	52 Days	B		20
106[b]	Unk	Endothelioma	Unk	Unk	Unk		22
107	Lymphatics	Angioendothelioma (Dabska-like tumor)	M	4	B	Synonyms: malignant endovascular papillary angioendo-thelioma, papillary intralymphatic angioendothelioma	2
Musculoskeletal System							
108	Scapula	Sarcoma	F	Unk[b]	M		22
109	Unk	Sarcoma	M	15	M		18

Case #	Location	Diagnosis	Sex	Age (Years) at Diagnosis	Malignant or Benign	Comments[a]	Reference
110	Maxilla	Odontoma	Unk[b]	Unk[b]	B		10
Respiratory System							
111	Nasal cavity	Cartilaginous fibromyxoma (nasal polyp)	M	11	B	Tumor near molar projection of palantine bone	26
112	Nose	Fibromyxomatous polyposis	F	10	B	Polyp obstructed almost entire upper respiratory tract	14
113	Nasopharynx	Carcinoma	F	10	M	Tumor had intracranial/skull cavity extension	3
Hematopoietic System							
114	Abdominal cavity	Anaplastic large cell lymphoma (T-cell phenotype)	M	35	M	Negative for retroviruses, no other virus isolated	6
115[b]	Bone marrow	Erythroleukemia	M	1	M	Experimental infection: bovine C-type virus	4
116[b]	Bone marrow	Erythroleukemia	M	1	M	Experimental infection: bovine C-type	4
Central Nervous System							
117[b]	Brain	Brain tumor of unknown type	Unk	Unk	Unk		17

[a] HBV, hepatitis B virus; HCV, hepatitis C virus; NANBH, non-A, non-B hepatitis virus; HIV, human immunodeficiency virus

[b] Not included in statistical analysis

[c] Unk, unknown

Table 2

Age at diagnosis, sex, and malignancy by system.

	N*	Age (years)** (n=91)	Sex (female %)*** (n=95)	Malignant %*** (n=99)
Urogenital	49	(48) 35.4±1.3	(49) 100%	(49) 6%
Integumentary	18	(12) 25.1±4.0[a]	(14) 71%	(18) 5%
Endocrine	13	(13) 32.1±3.3	(13) 54%[a]	(13) 7%
Alimentary	11	(11) 30.5±2.9	(11) 36%[a]	(11) 45%[a,b,c]
Cardiovascular	6	(4) 24.2±6.8[a]	(5) 20%[a]	(5) 0%[d]
Respiratory	3	(3) 10.3±0.3[a,b,c,d]	(3) 67%	(3) 33%

* N based on cases with adequate information available

** Age was compared using Kruskal-wallis test

*** Sex and Benign/Malign were compared using Fisher's Exact Test

[a] $p<0.05$ compared with urogenital group

[b] $p<0.05$ compared with integumentary group

[c] $p<0.05$ compared with endocrine group

[d] $p<0.05$ compared with alimentary group

Table 3

Age at diagnosis and sex for malignancy.

Variable	N*	Benign (n=89)	Malignant (n=14)	*p*
Age (years)**	93	32.4 ± 1.2 (81)	25.4 ± 3.0 (12)	0.050
Sex (female %)***	98	80% (84)	50% (14)	0.038

* N based on cases with adequate information available

** Age was compared using Mann-Whitney test

*** Sex was compared using Fisher's Exact Test