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A retrospective survey on canine intracranial tumors between 2007 and 2017

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ABSTRACT. To clarify the prevalence of canine intracranial tumors in Japan, a retrospective study was performed using data on 186 canine intracranial tumors. Of 186 cases, 159 cases (85.5%) were primary and 27 cases (14.5%) were secondary intracranial tumors. Among primary intracranial tumors, meningioma (50.9%) was the most common, followed by glial tumors (21.4%) and primary intracranial histiocytic sarcoma (12.6%). These 3 tumors were most frequently found in middle-aged to elderly dogs without any sex predilection. Regarding glial tumors, the incidence of oligodendroglial tumors (79.4%) was higher than that of astrocytic tumors (17.6%). A significant breed predisposition ($P<0.05$) was observed for meningioma in Rough Collie, Golden Retriever, Miniature Schnauzer, and Scottish Terrier; for glial tumors in Bouvier de Flandres, French Bulldog, Newfoundland, Bulldog, and Boxer; for primary intracranial histiocytic sarcoma in Pembroke Welsh Corgi, Siberian Husky, and Miniature Schnauzer. The high incidence of oligodendroglial tumors in dogs and the breed predisposition for primary intracranial histiocytic sarcoma in Pembroke Welsh Corgi have not been reported in previous epidemiological studies on canine tumors. Since the incidence of intracranial tumors was vary among dog breeds, the present results demonstrate the uniqueness of the canine breed population in Japan.

KEY WORDS: brain tumor, dog, epidemiology, histopathology, intracranial tumor

Intracranial tumors include a large group of different benign and malignant tumors arising from the brain parenchyma and its surrounding structures [11]. These tumors are an important cause of morbidity and mortality in companion animals, particularly dogs. The increased use of computed tomography (CT) and magnetic resonance imaging (MRI), along with pathological examinations of biopsy samples, have increased the accuracy of antemortem diagnoses of canine intracranial tumors in recent years. However, the epidemiology of these tumors in dogs remains unclear, and few studies have investigated the incidence of canine intracranial tumors in the United States and United Kingdom [5, 6, 21–23]. Previous reports revealed that the incidence of canine intracranial tumors varied between 0.01% [21] and 4.5% [8, 23].

According to the World Health Organization (WHO) classification of tumors in domestic animals, intracranial tumors are divided into neuroepithelial, meningothelial, hematopoietic, and other tumors based on the anatomical location and tissue type [11]. Among these tumors, meningioma is the most common primary intracranial tumor in dogs, followed by glial tumors, including astrocytoma, oligodendroglioma, and oligoastrocytoma [8, 22]. Certain breeds are predisposed to specific types of intracranial tumors: meningioma in dolichocephalic breeds, such as German Shepherd dog and Rough Collie, and glial tumors in brachycephalic breeds, including Boxer and Boston Terrier [4, 8, 17, 23].

There are large differences in the popularity of dog breeds and breeding systems among countries, which may potentially influence the incidence of intracranial tumors. Therefore, it is important to collect data from different countries in order to obtain a better understanding of the epidemiology of canine intracranial tumors. The incidence of intracranial tumors in the dog has not yet been examined in Japan. The aim of the present study was to investigate the prevalence of primary and secondary canine intracranial tumors and clarify the breed, age, and occurrence site predilections for specific intracranial tumors in Japan.

MATERIALS AND METHODS

The histopathological database maintained in the Laboratory of Veterinary Pathology, Graduate School of Agricultural and

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Life Sciences, The University of Tokyo was searched for dogs with a diagnosis of intracranial tumors between 2007 and 2017. As a referral diagnostic center of neuropathology, intracranial tumor cases were submitted to our institution from veterinary clinics across Japan, covering a wide geographic region (Honshu, Shikoku, and Kyusyu islands). Biopsy and necropsy cases with a diagnosis of intracranial tumors occurring in the brain, pituitary gland, and meninges were both examined. Parameters reviewed were breed, age at the time of diagnosis, sex, anatomical site of the tumor, and histological type. The anatomical site of the tumor was recorded based on CT, MRI, and/or post-mortem examinations. The ages of dogs were categorized as 0–3, >3–5, >5–7, >7–9, >9–11, >11–13, >13–15, and >15.

Histology slides were reviewed and diagnosed on consensus of 3 Japanese College of Veterinary Pathologists board-certified pathologists (T.E.K, J.K.C., and K.U.), according to the WHO classification of domestic animals [11]. Intracranial tumors were divided into primary and secondary. Primary tumors were defined as those without any extracranial tumor occurrence and were classified as per the established criteria. Lymphoma and histiocytic sarcoma were also included in primary intracranial tumors if the lesions were confined to the brain. Secondary intracranial tumors were defined as those metastasized from other parts of the body. Tumors that originated from neural and non-neural tissues adjacent to the brain and affected the brain by expansion were also included in the secondary intracranial tumor category. The presence of other tumors unrelated to intracranial tumors was confirmed based on a clinical or postmortem examination. Additionally, immunohistochemistry was performed as deemed necessary to confirm the histopathological diagnoses and subtyping of intracranial tumors. Primary antibodies are detailed in Table 1.

Statistical analyses were performed using IBM® SPSS® Statistics version 23 (IBM SPSS, Armonk, NY, USA). Pearson's chi-squared test and likelihood ratio test were used to investigate the breed and sex predisposition in canine intracranial tumors. Results were reported as odds ratios (OR) with its associate confidence interval (CI), and $P<0.05$ was considered to be significant. Additionally, cases of choroid plexus tumors, intracranial lymphomas, embryonal tumors, pituitary tumors, and secondary intracranial tumors were excluded from statistical analyses due to the small number of samples.

RESULTS

During the 11 years that the study covered, 9,270 canine cases were histopathologically examined and included 4,580 males (2,168 neutered and 2,412 intact), 4,571 females (2,666 neutered and 1,905 intact), and 119 unknown. A total of 186 cases (2.0%) were diagnosed with intracranial tumors; 159 cases (85.5%) were primary and 27 cases (14.5%) were secondary intracranial tumors. The relative frequency, age, and sex distributions of each tumor type were summarized in Table 2. The three most common histopathological types of primary intracranial tumors were meningioma (n=81; 50.9%), glial tumors (n=34; 21.4%), and histiocytic sarcoma (n=20; 12.6%). Primary intracranial tumors were most frequently found between the ages of 11 and 13 years, representing 29.4% (n=45) of all canine primary intracranial tumor cases. There was no significant sex predilection for primary intracranial tumors (P=0.990).

One hundred and twenty-seven dog breeds were represented during the term. Miniature Dachshund (n=1,420; 15.3%), mixed breed dog (n=852; 9.2%), Toy Poodle (n=527; 5.7%), Shih Tzu (n=456; 4.9%), Chihuahua (n=443; 4.8%), Golden Retriever (n=426; 4.6%), Pembroke Welsh Corgi (n=422; 4.6%), Labrador Retriever (n=406; 4.4%), Beagle (n=341; 3.7%), Shiba-Inu (n=339; 3.7%), Yorkshire Terrier (n=320; 3.5%), and French Bulldog (n=293; 3.2%) were the most common breeds. Other dog breeds were represented at less than 3%. French Bulldog (n=25 of 293; $P<0.0001$), Rough Collie (n=2 of 6; $P<0.0001$), Miniature Bull Terrier (n=1 of 2; $P<0.0001$), Bouvier des Flandres (n=1 of 4; P=0.0003), Miniature Schnauzer (n=11 of 241; P=0.0006), Pembroke Welsh Corgi (n=16 of 422; P=0.0008), Golden Retriever (n=16 of 426; P=0.0009), Siberian Husky (n=3 of 33; P=0.0011), Miniature Dachshund (n=13 of 1,420; P=0.0171), Newfoundland (n=1 of 9; P=0.0299), and Basset Hound (n=1 of 10; P=0.0435) were at a higher risk of developing primary intracranial tumors than the rest of the canine population.

Table 1. Immunohistochemical markers used in the diagnosis and subclassification of specific tumor types

Tumor type	Immunohistochemical markers
Meningioma	Cytokeratin and E-cadherin
Glial tumor	GFAP and Olig2
Primary intracranial histiocytic sarcoma	CD204, HLA-DR, and Iba1
Choroid plexus tumor	Cytokeratin and E-cadherin
Ependymal tumor	GFAP
Intracranial lymphoma	CD3 and CD20
Embryonal tumor	β IIItubulin, doublecortin, GFAP, nestin, and synaptophysin

GFAP, glial fibrillary acidic protein; Iba1, ionized calcium-binding adapter molecule 1; Olig2, oligodendrocyte lineage transcription factor 2. Primary antibodies: β IIItubulin (clone 5G8; Promega Corp., Madison, WI, USA), CD3 (polyclonal antibody (pAb); Dako, Tokyo, Japan), CD20 (pAb; Biocare Medical, Concord, CA, USA), CD204 (clone SRA-C6; Trans Genic, Kobe, Japan), cytokeratin (clone AE1/AE3; Dako), doublecortin (pAB; Santa Cruz Biotechnology, Santa Cruz, CA, USA), E-cadherin (clone 36/E-Cadherin; BD Biosciences, San Jose, CA, USA), GFAP (pAB; Dako), HLA-DR (clone TAL 1B5; Santa Cruz Biotechnology), Iba1 (pAb; Wako, Osaka, Japan), nestin (pAB; Immuno-Biological Laboratories, Fujioka, Japan), Olig2 (pAB; Millipore, Billerica, MA, USA), and synaptophysin (clone DAK-SYNAP; Dako).

Table 2. Relative frequency, age, and sex distributions of primary and secondary intracranial tumors in the dog

Tumor type	Number of cases (% cases within primary intracranial tumors)	Age (years)									Mean age (years)	Sex			Sex ratio (♂:♀)
		0–3	>3–5	>5–7	>7–9	>9–11	>11–13	>13–15	>15	ND [b)]		Male (neutered)	Female (neutered)	ND [b)]	
Primary intracranial tumors	159	2	5	10	25	36	45	23	7	6	10.3	76 (28)	76 (44)	7	1:1
Meningioma	81 (50.9%)	0	0	2	9	22	25	15	5	3	11.2	40 (13)	38 (23)	3	1:1.05
Glial tumor	34 (21.4%)	1	3	3	8	5	9	3	1	1	9.1	15 (6)	18 (11)	1	1:1.05
PIHS [a)]	20 (12.6%)	0	0	1	4	5	6	4	0	0	10.5	10 (5)	10 (7)	0	1:1
Choroid plexus tumor	8 (5.0%)	1	1	3	1	0	2	0	0	0	6.5	2 (0)	5 (2)	1	1:2.5
Intracranial lymphoma	7 (4.4%)	0	0	1	1	2	1	0	0	2	9.3	3 (2)	2 (0)	2	1:0.66
Embryonal tumor	6 (3.8%)	0	1	0	1	1	2	1	0	0	10.1	4 (1)	2 (0)	0	1:0.5
Pituitary tumor	3 (1.9%)	0	0	0	1	1	0	0	1	0	10.8	2 (1)	1 (1)	0	1:0.5
Secondary intracranial tumor	27	1	0	3	2	5	3	10	2	1	11.0	12 (4)	13 (8)	2	1:1.08
All intracranial tumors	186	3	5	13	27	41	48	33	9	7	10.4	88 (32)	89 (52)	9	1:0.99

a) PIHS, primary intracranial histiocytic sarcoma. b) ND, no data.

Meningioma

Meningioma represented 50.9% of primary intracranial tumors, with an overall prevalence of 0.87% of the total population. Meningiomas were most frequently found between the ages of 11 and 13 years, representing 32.1% (n=25) of all canine meningioma cases (Table 2). There was no sex predilection (P=0.827). Statistical analyses showed that Rough Collie, Golden Retriever, Miniature Schnauzer, and Scottish Terrier had a significantly higher risk of meningioma (P<0.05) than the rest of the total canine population (Table 3). Occurrence sites of meningiomas were recorded in 63 dogs and included the cerebrum in 50 cases (79.4%), cerebellum in 6 cases (9.5%), brain stem in 5 cases (7.9%), and multiple regions in 2 cases (3.2%). As for cerebral meningiomas, 34 cases (68.0%) were located in the frontal region including the olfactory bulb and frontal lobe, 5 cases (10.0%) were located in the parietal lobe, and 3 cases (6.0%) were located in the temporal lobe. In 8 cases (16.0%), tumors were located in multiple cerebral lobes.

Histopathological subtypes of meningioma were identified in 73 of the 81 cases, according to the WHO classification of tumors in domestic animals [11]. Forty cases (54.8%) were diagnosed as benign and 33 cases (45.2%) as anaplastic. Of benign meningiomas, the meningothelial type was the most common (n=23; 57.5%), followed by the transitional (n=6; 15.0%), granular cell (n=4; 10.0%), psammomatous (n=3; 7.5%), fibrous (n=2; 5.0%), and papillary (n=2; 5.0%) types. The myxoid and angiomatous types were not found in the present study.

Glial tumors

Glial tumors represented 21.4% of primary intracranial tumors, with an overall prevalence of 0.37% in the total population. Among glial tumors, the most common histopathological subtype was oligodendroglial tumors (79.4%; 2 oligodendrogliomas and 25 anaplastic oligodendrogliomas), followed by astrocytic tumors (17.6%; 1 astrocytoma, 1 anaplastic astrocytoma, and 4 glioblastomas) and gliomatosis cerebri (2.9%; 1 case). Glial tumors were most frequently found between the ages of 11 and 13 years, representing 27.3% (n=9) of all canine glial tumor cases (Table 2). The mean ages of dogs with oligodendroglial tumors and astrocytic tumors were 9.2 and 8.7 years, respectively. There was no sex predilection (P=0.597). Statistical analyses showed that Bouvier de Flandres, French Bulldog, Newfoundland, Bulldog, and Boxer had a higher risk of glial tumors (P<0.05) than the rest of the total canine population (Table 4). Information on tumor occurrence sites was available for 29 out of 34 glial tumor cases. Among the 29 cases, glial tumors mostly occurred in the cerebrum (n=27; 93.1%), while others were in multiple regions (n=2; 6.9%). Regarding cerebral glial tumors, the frontal lobe was the most commonly affected site (n=11; 40.7%), followed by the temporal (n=7; 25.9%), parietal (n=2; 7.4%), piriform (n=2; 7.4%), and occipital (n=1; 3.7%) lobes, respectively. Four cases (14.8%) had a diffuse lesion widely invading the cerebrum.

Primary intracranial histiocytic sarcoma

Primary intracranial histiocytic sarcoma (PIHS) represented 12.6% of primary intracranial tumors, with an overall prevalence of 0.22% in the total population. These tumors were most frequently found between the ages of 11 and 13 years, representing 30.0% (n=6) of all canine PIHS cases. There was no sex predilection (P=0.996) (Table 2). Statistical analyses showed that Pembroke Welsh Corgi, Siberian Husky, and Miniature Schnauzer had a significantly higher risk of PIHS (P<0.05) than the rest of the total canine population (Table 5). Information on the tumor location was available in 16 out of 20 PIHS cases. In the 16 cases, PIHS only occurred in the cerebrum (n=16; 100.0%). The temporal lobe was the most commonly affected (n=4; 25.0%), followed by the frontal (n=3; 18.8%), parietal (n=2; 12.5%), and occipital (n=2; 12.5%) lobes. Five cases (31.3%) had diffuse lesions in wide areas of the cerebrum.

Table 3. Prevalence and risk of meningioma in each dog breed

Breed	No. of dogs examined (A)	No. of primary intracranial tumor (B)	No. of meningioma (C)	% Meningioma of the breed within the total number of meningioma (C/81 × 100)	% Meningioma within the breed (C/A × 100)	% Meningioma within all primary intracranial tumors of the breed (C/B × 100)	Odds ratio	95% CI	*P* value [a)]
Rough Collie	6	2	2	2.5	33.3	100.0	58.133	10.496–321.982	<0.001†
Golden Retriever	426	16	14	17.3	3.3	87.5	4.451	2.481–7.985	<0.001†
Miniature Schnauzer	241	11	7	8.6	2.9	63.6	3.620	1.650–7.943	<0.001†
Scottish Terrier	13	1	1	1.2	7.7	100.0	9.559	1.228–74.392	0.008†
Chihuahua	443	8	7	8.6	1.6	87.5	1.899	0.870–4.147	0.102
Labrador Retriever	406	9	1	1.2	0.2	11.1	0.271	0.038–1.953	0.165
Siberian Husky	33	3	1	1.2	3.0	33.3	3.577	0.483–26.496	0.182
Toy Poodle	527	9	7	8.6	1.3	77.8	1.577	0.723–3.440	0.248
Yorkshire Terrier	320	2	1	1.2	0.3	50.0	0.348	0.048–2.506	0.272
French Bulldog	293	25	1	1.2	0.3	4.0	0.381	0.053–2.746	0.320
German Shepherd dog	47	1	1	1.2	2.1	100.0	2.485	0.338–18.236	0.354
Miniature Dachshund	1,420	13	10	12.3	0.7	76.9	0.777	0.400–1.510	0.456
Papillion	200	1	1	1.2	0.5	100.0	0.565	0.078–4.078	0.566
Shiba-Inu	339	3	2	2.5	0.6	66.7	0.665	0.163–2.717	0.567
Pug	157	2	2	2.5	1.3	100.0	1.476	0.359–6.058	0.587
Shetland Sheepdog	260	4	3	3.7	1.2	75.0	1.337	0.419–4.263	0.623
West Highland White Terrier	71	1	1	1.2	1.4	100.0	1.628	0.223–11.867	0.627
Pembroke Welsh Corgi	422	16	3	3.7	0.7	18.8	0.805	0.253–2.561	0.713
Jack Russell Terrier	158	2	1	1.2	0.6	50.0	0.719	0.099–5.200	0.743
Bernese Mountain dog	92	1	1	1.2	1.1	100.0	1.250	0.172–9.078	0.825
Mixed breed dog	852	12	8	9.9	0.9	66.7	1.084	0.520–2.256	0.830
Maltese	209	2	2	2.5	1.0	100.0	1.099	0.268–4.500	0.896
Shih Tzu	456	5	4	4.9	0.9	80.0	1.004	0.366–2.756	0.994
Total	7,391	149	81	100.0					

a) Breeds with a $P<0.05$ (†) were considered to have a significantly higher risk of the occurrence of meningioma than the rest of the evaluated population.

Table 4. Prevalence and risk of glial tumors in each dog breed

Breed	No. of dogs examined (A)	No. of primary intracranial tumors (B)	No. of glial tumors [a)] (C)	% Glial tumors of the breed within the total number of glial tumors (C/34 × 100)	% Glial tumors within the breed (C/A × 100)	% Glial tumors within all primary intracranial tumors of the breed (C/B × 100)	Odds ratio	95% CI	*P* value [b)]
Bouvier des Flandres	4	1	1 (1 GC)	2.9	25.0	100.0	93.263	9.455–919.891	<0.001†
French Bulldog	293	25	22 (1 GB, 2 O, 19 AO)	64.7	7.5	88.0	60.649	29.708–123.814	<0.001†
Newfoundland	9	1	1 (1 AO)	2.9	11.1	100.0	34.955	4.252–287.383	<0.001†
Bulldog	17	1	1 (1 AO)	2.9	5.9	100.0	17.462	2.250–135.508	<0.001†
Boxer	18	1	1 (1 A)	2.9	5.6	100.0	16.433	2.125–127.084	<0.001†
Boston Terrier	83	1	1 (1 AO)	2.9	1.2	100.0	3.383	0.457–25.028	0.205
Mixed breed dog	852	12	1 (1 GB)	2.9	0.1	8.3	0.299	0.041–2.186	0.206
Shih Tzu	456	5	1 (1 GB)	2.9	0.2	20.0	0.585	0.080–4.285	0.593
Chihuahua	443	8	1 (1 AA)	2.9	0.2	12.5	0.603	0.082–4.418	0.615
Pembroke Welsh Corgi	422	16	1 (1 GB)	2.9	0.2	6.3	0.634	0.087–4.650	0.652
Labrador Retriever	406	9	2 (2 AO)	5.9	0.5	22.2	1.366	0.326–5.721	0.668
Yorkshire Terrier	320	2	1 (1 AO)	2.9	0.3	50.0	0.847	0.115–6.231	0.870
Total	3,323	82	34 (1 A, 1 AA, 4 GB, 2 O, 25 AO, 1 GC)	100.0					

a) A, astrocytoma; AA, anaplastic astrocytoma; GB, glioblastoma; O, oligodendroglioma; AO, anaplastic oligodendroglioma; GC, gliomatosis cerebri. b) Breeds with a $P<0.05$ (†) were considered to have a significantly higher risk of the occurrence of glial tumors than the rest of the evaluated population.

Table 5. Prevalence and risk of primary intracranial histiocytic sarcoma (PIHS) in each dog breed

Breed	No. of dogs examined (A)	No. of primary intracranial tumors (B)	No. of PIHS (C)	% PIHS of the breed within the total number of PIHS (C/20 × 100)	% PIHS within the breed (C/A × 100)	% PIHS within all primary intracranial tumors of the breed (C/B × 100)	Odds ratio	95% CI	*P* value [a)]
Pembroke Welsh Corgi	422	16	10	50.0	2.4	62.5	21.451	8.879–51.825	<0.001†
Siberian Husky	33	3	1	5.0	3.0	33.3	15.162	1.970–116.670	<0.001†
Miniature Schnauzer	241	11	2	10.0	0.8	18.2	4.189	0.967–18.156	0.037†
Beagle	341	2	2	10.0	0.6	100.0	2.921	0.675–12.638	0.133
Labrador Retriever	406	9	2	10.0	0.5	22.2	2.433	0.563–10.521	0.219
French Bulldog	293	25	1	5.0	0.3	4.0	1.615	0.215–12.102	0.638
Toy Poodle	527	9	1	5.0	0.2	11.1	0.873	0.117–6.533	0.895
Golden Retriever	426	16	1	5.0	0.2	6.3	1.093	0.146–8.183	0.931
Total	2,689	91	20	100.0					

a) Breeds with a *P*<0.05 (†) were considered to have a significantly higher risk of PIHS than the rest of the evaluated population.

Choroid plexus tumors

Choroid plexus tumors represented 5.0% of primary intracranial tumors, with an overall prevalence of 0.09% in the total population. These tumors were histologically classified into 5 choroid plexus papillomas (62.5%) and 3 choroid plexus adenocarcinomas (37.5%). Choroid plexus tumors were most frequently found between the ages of 5 and 7 years, representing 37.5% (n=3) of all canine choroid plexus tumor cases (Table 2). This tumor was identified in mixed breed dog (n=2; 25.0%), followed by Golden Retriever (n=1; 12.5%), Flat Coated Retriever (n=1; 12.5%), Labrador Retriever (n=1; 12.5%), Miniature Bull Terrier (n=1; 12.5%), Jack Russell Terrier (n=1; 12.5%), and Toy Poodle (n=1; 12.5%). Information on tumor locations was available for 7 out of 8 cases. Among the 7 cases, the tumor occurred most commonly in the fourth ventricle (n=4; 57.1%), followed by the lateral (n=2; 28.6%) and third (n=1; 14.3%) ventricles.

Intracranial lymphoma

Intracranial lymphoma represented 4.4% of primary intracranial tumors, with an overall prevalence of 0.08% in the total population. Five cases were immunohistochemically classified as T- or B-cell types. Of the 5 cases, 4 cases were T-cell lymphoma and 1 case was B-cell lymphoma. Labrador Retriever was the most affected breed (n=3; 42.9%), followed by Siberian Husky (n=1; 14.3%), Basset Hound (n=1; 14.3%), Miniature Schnauzer (n=1; 14.3%), and Pembroke Welsh Corgi (n=1; 14.3%). Canine intracranial lymphoma occurred most commonly in the cerebrum (n=6 of 7; 85.7%), followed by the cerebellum (n=3; 42.9%), mesencephalon (n=1; 14.3%), and medulla oblongata (n=1; 14.3%). Six cases (85.7%) had multiple lesions widely invading the brain and 1 case (14.3%) had a focal lesion in the brain.

Other intracranial tumors

Embryonal tumors represented 3.8% of primary intracranial tumors, with a prevalence of 0.06% among the total population. These tumors were histologically classified into 3 olfactory neuroblastomas (50.0%), 1 neuroblastoma (16.7%), 1 medulloblastoma (16.7%), and 1 primitive neuroectodermal tumor (16.7%). Among these tumors, Miniature Dachshund was the most affected breed (n=3; 50.0%), followed by French Bulldog (n=1; 16.7%), Miniature Schnauzer (n=1; 16.7%), and Shetland Sheepdog (n=1; 16.7%).

Pituitary tumors represented 1.9% of primary intracranial tumors, with a prevalence of 0.03% among the total population. These tumors were histologically classified into 1 pituitary adenoma (33.3%) and 2 pituitary adenocarcinomas (66.7%). The tumor was identified in mixed breed dog (n=1; 33.3%), Pembroke Welsh Corgi (n=1; 33.3%), and Shiba-Inu (n=1; 33.3%).

Secondary intracranial tumors

Secondary intracranial tumors represented 14.5% of all intracranial tumors, with an overall prevalence of 0.29% among the total population. There were 16 metastatic/invasive sarcomas including round cell tumors (59.3%) and 11 metastatic carcinomas (40.7%). The most common secondary intracranial tumor was lymphoma (n=8; 29.6%), followed by osteosarcoma (n=4; 14.8%), hemangiosarcoma (n=2; 7.4%), histiocytic sarcoma (n=2; 7.4%), and mammary gland adenocarcinoma (n=2; 7.4%). These tumors were most frequently found between the ages of 13 and 15 years, representing 38.5% (n=10) of all canine secondary intracranial tumor cases (Table 2). Sex predilection was not detected (*P*=0.837). Secondary intracranial tumors were identified in 15 different breeds. Those most commonly represented were mixed breed dog (n=6; 22.2%), followed by Labrador Retriever (n=3; 11.1%), Beagle (n=2; 7.4%), Chihuahua (n=2; 7.4%), Miniature Dachshund (n=2; 7.4%), Pembroke Welsh Corgi (n=2; 7.4%), and Shiba-Inu (n=2; 7.4%). Information on tumor locations was available in 22 out of 27 secondary intracranial tumor cases. Tumors most commonly affected the cerebrum (n=19; 86.4%), followed by the cerebellum (n=7; 31.8%). Ten cases (45.5%) had multiple lesions widely invading the brain.

DISCUSSION

The incidence of canine intracranial tumors has been reported to vary among studies performed in different regions and periods of time. A study on dogs living in Alameda and Contra Costa County of California (1963–1973) reported that the incidence of canine intracranial tumors was 14.5 cases/100,000 [21], while a study in the United Kingdom (1997–1998) reported an incidence of 20 cases/100,000 [4]. In contrast, another recent retrospective study suggested that the incidence of intracranial tumors was markedly higher than originally expected [23]. A retrospective single-center study from the University of Pennsylvania indicated that in a population of 9,574 dogs undergoing necropsy, 4.5% had primary intracranial tumors [23]. In the present study, the incidence of canine intracranial tumors (186 cases/9,270, 2.0%) was closer to the latest findings. However, since this was a single-institution study, there may be a bias of sample collection, such as the proportion of neuropathology cases to all cases, which may be higher at our institution than at other institutions in Japan. To the best of our knowledge, this is the first survey on canine intracranial tumors in Japan.

In the present study, the relationship between the incidence of primary intracranial tumors and dog breeds was examined. Previous studies reported a predisposition for the occurrence of primary intracranial tumors in certain large-sized dog breeds, such as Boxer, Golden Retriever, Old English Sheep dog, and Doberman Pinscher [4, 7, 15, 21, 23]. In contrast to previous findings, the present study showed the predisposed occurrence of primary intracranial tumors in small- and middle-sized breeds. This difference was considered to be associated with the breed population and breeding system in Japan where small- and middle- sized dogs are commonly bred [10].

The WHO classification of tumors of domestic animals is a simple and practical classification system for routine diagnosis; however, limited information is currently available on the clinical and molecular features of each tumor [11]. It has been an important reference for pathological diagnoses and epidemiological studies over the past two decades. In order to compare epidemiological findings with previous studies, this classification was adopted to classify intracranial tumors in the present study.

Meningioma is an extra-axial central nervous system tumor of arachnoid cap cells of the dura within the cranial space [8, 17]. Consistent with previous findings, meningioma was the most common intracranial tumor (50.9%) in dogs also represented in this study [17, 22, 23]. Some results in the present study, including the most commonly affected age (middle-aged to older dogs) and location (rostral cerebrum), were consistent with those in a previous study [17]. In humans, meningioma has a clear female predilection [12], which is considered to be associated with the expression of female hormone receptors in tumor cells [2]. Canine meningioma also expresses female hormone receptors [1, 13]; however, the sex predilection observed in human cases was not observed in the present or previous canine studies [17, 22, 24]. Based on the results of the present study, Golden Retriever, Miniature Schnauzer, and Rough Collie have a higher risk of developing meningioma than other dog breeds. This result is consistent with previous findings [22, 23, 27]. Moreover, the present study identified Scottish Terrier as a predisposed breed for meningioma, which has not been reported to date. Meningioma exhibits variable morphological patterns; however, its biological behaviors are generally considered to be benign in the dog with the exception of the anaplastic type [11]. In the present study, meningothelial (57.5%) and transitional (15.0%) meningiomas were the two major benign histological types in the dog. This result coincides with the findings obtained in a previous study on canine meningioma [19]. The incidence of anaplastic meningioma in the present study was 45.2% (33/73), which is higher than that of anaplastic meningioma (27.2%; 6/22) reported in a previous study [19].

Glial tumors are divided into astrocytic and oligodendroglial tumors [8, 11]. The incidence of glial tumors of 21.4% is slightly lower than that in other countries (36.6%). In the present study, glial tumors most commonly affected middle-aged to elderly dogs with no sex predilection. The most frequently affected area of the brain was the cerebrum, particularly the frontal lobe, which was consistent with previous findings [8, 23]. Boxer, Bulldog, Boston Terrier, English Bulldog, and Bullmastiff are known to be predisposed to glial tumors [8, 11, 22, 23]. The present study also identified brachycephalic breeds (French Bulldog, Bulldog, and Boxer) as those predisposed to developing glial tumors. Additionally, this study identified Newfoundland as a predisposed breed for glial tumors. Many of these breeds are Mastiff-type breeds [18, 20, 26]. Therefore, genetic factors are likely to be involved in the development of canine gliomas. The incidence of oligodendroglial tumors in the present study (79.4%) was markedly higher than that of astrocytic tumors, which was inconsistent with previous findings [22]. Boxer and Boston Terrier are known to have a higher risk of developing astrocytic tumors than other dog breeds [6, 8, 23]. Since only a small number of these breeds was included in the present study, the difference in the incidence of astrocytic tumors between Japan and other countries was considered to be caused by different breed populations.

PIHS originates from resident dendritic cells in either the meninges or choroid plexus [3, 9, 14, 16]. Although this tumor has been reported as an uncommon tumor in the dog (approximately 2.0%) [22, 23], it was the third most common tumor type in the present study (12.6%). PIHS most commonly affected middle-aged to elderly dogs with no sex predilection, which is consistent with previous findings [8, 22, 23]. We previously proposed that PIHS has a predilection for Pembroke Welsh Corgi [9, 25], and the present results statistically demonstrated that Pembroke Welsh Corgi has a significantly increased risk of PIHS. Moreover, the difference in the incidence of PIHS between the present results and previous findings [22, 23] was considered to be caused by the difference in the population number of this breed in each country.

In conclusion, the present cohort study provides the current estimated prevalence of canine primary and secondary intracranial tumors in Japan. Many of the characteristics of intracranial tumors in the present study are similar to those reported previously. However, a high incidence of oligodendroglial tumors and the predisposition of Pembroke Welsh Corgi to PIHS are novel results. Since the epidemiological features of intracranial tumors may differ among breed types, these novel results are unique to Japan.

However, there was a limitation and bias due to a small size of the study population. Epidemiological information on canine intracranial tumors obtained in the present study may help veterinarians to establish an accurate antemortem diagnosis of canine intracranial tumors.

CONFLICT OF INTEREST. The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this manuscript.

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