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Feline neurological diseases in a veterinary neurology referral hospital population in Japan

Yuya NAKAMOTO[1,2)]*, Takashi UEMURA[1)], Hiroki HASEGAWA[1)], Miwa NAKAMOTO[1)] and Tsuyoshi OZAWA[1)]

[1)]Kyoto Animal Referral Medical Center, 208-4, Shinarami, Tai, Kumiyama-cho, Kuze-gun, Kyoto 613-0036, Japan
[2)]Department of Bioartificial Organs, Institute for Frontier Life and Medical Sciences, Kyoto University, 53, Kawahara-cho, Sakyo-ku, Kyoto 606-8507, Japan

ABSTRACT. Many of the reports summarizing neurological disorders in cats considered only a limited disease group(s). There is only one large-scale survey on neurological disorders in cats based on the histopathological viewpoint. We described the localizations and frequencies of neurological diseases in a large population of cats that were referred to the Kyoto Animal Referral Medical Center between 2009 and 2016. We attempted to determine the localization of lesions at the time of the examination in each case and to classify the disease etiologies of these 276 cats with neurological disorders retrospectively. There were 174 cases with lesions in the brain region, 14 cases with lesions in the cervical cord region, 34 cases with lesions in the thoracolumbar cord region, and 54 cases with lesions in the peripheral neuromuscular region. High morbidity rates were observed in cases of idiopathic epilepsy and intracranial tumor in the brain region, spinal cord infarction in the cervical cord region, spinal cord infarction and spinal cord tumor in the thoracolumbar cord region, and peripheral vestibular dysfunction arising from otitis media/interna in the peripheral neuromuscular region. It was suggested that there is a higher number of brain diseases than spinal cord and peripheral neuromuscular diseases in cats. Idiopathic and neoplastic diseases were common in the brain region, vascular diseases were common in the spinal cord region, and infectious diseases were common in the peripheral neuromuscular region.

KEY WORDS: feline, incidence, Japan, neurological diseases, survey

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The accuracy of the antemortem diagnosis of neurological diseases in dogs and cats has been markedly improved since magnetic resonance imaging (MRI) was introduced into small animal practice for evaluation of the central nervous system. However, for the diagnosis of neurological diseases, it is important to exclude non-neurological diseases and to consider the localization of lesions and the diseases that might be present. To localize lesions, neurological examinations are important. To determine the differential diagnoses, it is necessary to understand the diseases' trends based on an accumulation of cases, in addition to the onset type (acute or chronic) and the presence or absence of progress [7]. Generally, neurological disorders are classified using the DAMNIT-V (or VITAMIN-D) method [3, 4, 13]. DAMNIT-V is a method for classifying diseases and is useful for the diagnosis of neurological diseases; it classifies them as degenerative (D), anomalous (A), metabolic (M), neoplastic (N), inflammatory (infectious/immune-mediated) (I), idiopathic (I), traumatic (T), and vascular (V) diseases [3, 4, 13].

Although the incidence rate of neurological disorders in cats in primary-care veterinary practices is not accurately known, it may be very low [15]. One survey report on neurological disorders in cats based on the histopathological viewpoint indicated that the incidence rate was approximately 10% [1]. However, the DAMNIT-V classification, which is considered clinically useful, was not used in that report. In addition, many of the reports summarizing neurological disorders in cats considered only a limited disease group(s) [2, 5, 6, 9, 12, 14, 16, 17, 19, 21, 23]. To the best of our knowledge, only two large-scale surveys on neurological disorders in dogs have been reported wherein the DAMNIT-V method was used for disease classification [6, 11]. Therefore, we thought it was necessary to summarize the basic data on cats using the DAMNIT-V classification.

In this study, we investigated the localizations and occurrence of various neurological disorders in cats based on the medical records dating from 2009 to 2016 from the Kyoto Animal Referral Medical Center (KyotoAR), a veterinary neurology referral hospital in Japan.

*Correspondence to: Nakamoto, Y.: yuya-nakamoto@kyotoar.com

MATERIALS AND METHODS

The medical records of cats admitted to the KyotoAR between November 2009 and October 2016 were examined for the localization and occurrence of neurological disorders. Clinical diagnoses were established by the authors Y. N., T. U., and H. H. based on the medical history, complete blood count, serum biochemistry profile, thoracic and abdominal radiographs, and neurological, MRI, cerebrospinal fluid, electrophysiological, histopathological, and genetic examinations. Cases with no detailed examination, cases of non-neurological diseases (such as orthopedic and cardiovascular diseases), and cases in which MRI was performed for treatment evaluation were excluded. Disease localizations were classified into two regions: the central nervous system region and the peripheral neuromuscular region. Lesions in the central nervous system region were classified according to their location as follows: forebrain, cerebellum, brain stem (midbrain, pons, and medulla oblongata), first cervical segment to fifth cervical segment (C1–5), sixth cervical to second thoracic segment (C6–T2), third thoracic–third lumbar segment (T3–L3), and fourth lumbar–third sacral segment (L4–S3) [4, 13]. However, because it was difficult to determine the localization of the lesions in many cases in this study, the central nervous system region was divided into brain (forebrain, cerebellum, and brain stem), cervical spinal cord (combining C1–5 and C6–T2), and thoracolumbar spinal cord (a combination of T3–L3 and L4–S3) regions. The classification of the diseases based on their clinical diagnosis was summarized using the DAMNIT-V classification method. The incidence of diseases in each part of the brain, the frequency of each disease in different cat breeds, the median age at diagnosis, and the age range at onset were surveyed.

RESULTS

The study population comprised 308 cases; of those, 32 cases were excluded and the remaining 276 cases, comprising 17 different cat breeds, that satisfied the inclusion criteria of this study were finally included. Among these, histopathological examinations were performed in 31 cases (11.2%). Crossbred cat was the most common breed (206 cases, 74.6%), followed by the American Shorthair (21 cases, 7.6%), the Russian Blue (9 cases, 3.3%), and the Scottish Fold (8 cases, 2.9%).

The lesions were localized in the brain region in 174 cases (63%), in the cervical cord region in 14 cases (5.1%), in the thoracolumbar cord region in 34 cases (12.3%), and in the peripheral neuromuscular region in 54 cases (19.6%).

The 174 cases with diseases localized in the brain region included 55 cases (31.4%) of neoplastic, 49 cases (29.1%) of idiopathic, 23 cases (13%) of inflammatory, 13 cases (7.3%) of degenerative, 12 cases (6.7%) of anomalous, 12 cases (6.7%) of vascular, 6 cases (3.4%) of metabolic, and 4 cases (2.2%) of traumatic diseases. Table 1 shows a breakdown of the above. Idiopathic epilepsy was diagnosed most frequently, accounting for 49 of the 176 cases (29.1%), followed by intracranial tumor (35 cases, 20.1%), extracranial tumor (14 cases, 8.0%), and intracranial influence of otitis media/interna (13 cases, 7.4%). Histopathological examinations were performed in 21 of these cases; there were 2 cases of GM-1 gangliosidosis (lysosomal storage diseases), 2 cases of feline infectious peritonitis virus encephalitis, 4 cases of lymphoma and of nasogastric carcinoma (intracranial infiltration of intranasal tumor) each, 1 case of osteosarcoma (others of extracranial tumor), 2 cases of lymphoma (intracranial tumor), and 6 cases of meningioma (intracranial tumor).

The 14 cases with diseases localized in the cervical cord region included 8 cases of vascular (57.4%), 2 cases of neoplastic (14.2%), and 1 case each (7.1%) of degenerative, anomalous, inflammatory, and traumatic diseases. Table 2 shows a breakdown of the above. Spinal cord infarction was diagnosed most commonly (8 cases, 57.4%). Histopathological examinations were performed in 3 of these cases; there were 1 case each of degenerative myelopathy, meningioma (spinal cord tumor), and anaplastic oligodendroglioma (spinal cord tumor).

The 34 cases with disease localized in the thoracolumbar cord region included 9 cases of neoplastic (26.6%), 9 cases of vascular (26.6%), 6 cases of diseases (17.6%), 5 cases of degenerative (14.6%), 4 cases of traumatic diseases (11.7%), and 1 case of an anomalous disease (2.9%). Table 3 gives a breakdown of these cases. Spinal cord tumor (9 cases, 26.6%) and spinal cord infarction (9 cases, 26.6%) were diagnosed most commonly. Histopathological examinations were performed in 4 of these cases; there were 2 cases each of lymphoma (spinal cord tumor) and meningioma (spinal cord tumor).

The 54 cases with diseases localized in the peripheral neuromuscular region included 35 cases (64.8%) of head-related peripheral nerve diseases, 10 cases (18.5%) of limb-related peripheral nerve diseases, and 9 cases (16.7%) of muscle diseases. The 35 cases of head-related peripheral nerve diseases included 29 cases (82.9%) of inflammatory and 6 cases (17.1%) of idiopathic diseases. All 10 cases of peripheral nerve diseases related to the limbs were difficult to classify because histopathological examination was not performed. Regarding the muscle diseases, there were 3 cases of inflammatory diseases (33.3%) and 1 case of a metabolic disease (11.1%); the remaining 5 cases were difficult to classify (55.6%). A breakdown of these data is given in Table 4. Facial/vestibular nerve disorder arising from otitis media/interna and Horner's syndrome (29 cases, 53.7%) were diagnosed most commonly in this region. Histopathological examinations were performed in 3 cases of diseases in the muscular region and all findings were that of polymyositis.

DISCUSSION

This retrospective study describes a large population of cats with neurological diseases based on the medical records from a veterinary neurology referral hospital in Japan. The disease frequencies per site were 63% in the brain region, 5.1% in the cervical cord region, 12.3% in the thoracolumbar cord region, and 19.6% in the peripheral neuromuscular region. Idiopathic and neoplastic

Table 1. Classification of the brain region diseases

	Disease name	Count	Disease rate (%)	Breed of cat	Count	Percentage of cat breed in disease group (%)	Median age (range)
D	LSD	8	4.5	CBC	8	100	0 y 5 m (0 y 3 m–0 y 10 m)
	CDS	5	2.8	CBC	3	60	16 y 1 m (12 y 5 m–16 y 11 m)
				Scottish Fold	1	20	
				Himalayan	1	20	
A	Hydrocephalus	5	2.8	CBC	2	40	0 y 5 m (0 y 3 m–0 y 10 m)
				Scottish Fold	1	20	
				Ragdoll	1	20	
				Russian Blue	1	20	
	Porencephalia	4	2.2	CBC	4	100	1 y 1 m (0 y 6 m–1 y 11 m)
	Others	3	1.7	-	-	-	-
M	HE/hypoxia, etc.	6	3.4	CBC	4	66.7	2 y 11 m (0 y 5 m–10 y 8 m)
				Siamese	1	16.6	
				ASH	1	16.6	
N	Extracranial tumor	14	8.0				
	IIIT	9	5.1	CBC	8	92.9	12 y 6 m (3 y 9 m–15 y)
				Russian Blue	1	7.1	
	Others	5	2.8	-	-	-	-
	PT	4	2.2	CBC	4	100	10 y 8 m (9 y 5 m–13 y)
	Metastatic tumor	2	1.1	CBC	2	100	12 y 6 m (11 y–14 y)
	Intracranial tumor	35	20.1	CBC	24	68.6	12 y 2 m (3 y 6 m–18 y 5 m)
				ASH	7	20	
				Others	4	11.4	
I	IFE	23	13.2				
	FIPE	5	2.8	Somali	1	20	0 y 5 m (0 y 5 m–0 y 7 m)
				Maine Coon	1	20	
				Russian Blue	1	20	
				Abyssinian	1	20	
				CBC	1	20	
	OM/OI	13	7.4	CBC	11	84.8	8 y 2 m (0 y 4 m–14 y 7 m)
				Singapura	1	7.6	
				Tonkinese	1	7.6	
	Others	5	2.8	-	-	-	-
Id	IE	49	29.1	CBC	33	67.6	4 y 11 m (0 y 5 m–14 y 6 m)
				ASH	7	14.2	
				NFC	4	8.1	
				Russian Blue	2	4	
				Others	3	6.1	
T	Falling	4	2.2	CBC	3	75	6 y 9 m (0 y 3 m–8 y 7 m)
				Scottish Fold	1	25	
V	FI	6	3.4	CBC	5	83.4	11 y 3 m (3 y–16 y 5 m)
				ASH	1	16.6	
	BSI	5	2.8	Persian	2	40	10 y 11 m (7 y 0 m–14 y 7 m)
				CBC	2	40	
				Chinchilla	1	20	
	CH	1	0.5	CBC	1	100	12 y
	Total	174	100				

D, degenerative disease; A, anomalous disease; M, metabolic disease; N, neoplastic disease; I, inflammatory disease; Id, idiopathic disease; T, traumatic disease; V, vascular disease; LSD, lysosomal storage diseases; CDS, cognitive dysfunction syndrome; HE, hepatic encephalopathy; IIIT, intracranial infiltration of intranasal tumor; PT, pituitary tumor (macroadenoma); IFE, infectious encephalitis; FIPE, feline infectious peritonitis virus encephalitis; OM/OI, otitis media/interna spreading intracranially; IE, Idiopathic epilepsy (including unknown epilepsy); FI, forebrain infarction; BSI, brain stem infarction; CH, cerebral hemorrhage; CBC, crossbred cats; ASH, American shorthair; NFC, Norwegian forest cat; y, year; m, month.

Table 2. Classification of diseases in the cervical cord region

	Disease name	Count	Disease rate (%)	Breed of cat	Count	Percentage of cat breed in disease group (%)	Median age (range)
D	DM	1	7.1	CBC	1	100	17 y
A	Syringomyelia	1	7.1	CBC	1	100	0 y 3 m
N	Spinal cord tumor	2	14.2	CBC	2	100	9 y 6 m (9 y–10 y 7 m)
I	NMM	1	7.1	CBC	1	100	1 y 8 m
T	Falling	1	7.1	CBC	1	100	0 y 3 m
V	SCI	8	57.4	CBC	6	75	9 y 6 m (3 y 8 m–15 y 10 m)
				Russian Blue	1	12.5	
				Persian	1	12.5	
	Total	14	100		14		

D, degenerative disease; A, anomalous disease; N, neoplastic disease; I, inflammatory disease; T, traumatic disease; V, vascular disease; DM, degenerative myelopathy; NMM, noninfectious meningomyelitis; SCI, spinal cord infarction; CBC, crossbred cats; y, year; m, month.

Table 3. Classification of diseases in the thoracolumbar cord region

	Disease name	Count	Disease rate (%)	Breed of cat	Count	Percentage of cat breed in disease group (%)	Median age (range)
D	IVDH	5	14.6	CBC	4	80	9 y 6 m (6 y 8 m–18 y)
				Munchkin	1	20	
A	VM	1	2.9	CBC	1	100	2 y 7 m
N	Spinal cord tumor	9	26.6	CBC	7	77.8	10 y 2 m (7 y 7 m–20 y)
				ASH	1	11.1	
				Scottish Fold	1	11.1	
I	IMM	6	17.6				
	BMM	3	8.3	CBC	3	100	3 y 6 m (0 y 11 m–9 Y 6 m)
	FIPMM	3	8.3	Bengal	1	33.3	0 y 10 m (0 y 7 m–1 y 1 m)
				Russian Blue	1	33.3	
				Persian	1	33.3	
T	Falling	4	11.7	CBC	3	75	2 y 6 m (0 y 2 m–8 y)
				Russian Blue	1	25	
V	SCI	9	26.6	CBC	8	88.9	8 y 9 m (2 y 7 m–17 y)
				Somali	1	11.1	
	Total	34	100		34		

D, degenerative disease; A, anomalous disease; N, neoplastic disease; I, inflammatory disease; T, traumatic disease; V, vascular disease; IVDH, intervertebral disc herniation; VM, vertebral malformation; IMM, infectious meningomyelitis; BMM, bacterial meningomyelitis; FIPMM, feline infectious peritonitis virus meningomyelitis; SCI, spinal cord infarction; CBC, crossbred cats; ASH, American shorthair; y, year; m, month.

were the most common diseases in the brain region, vascular diseases were the most common in the spinal cord region, and infectious diseases were the most common in the peripheral neuromuscular region. Crossbred cat was the most common breed (74.6%), followed by American Shorthair (7.6%), Russian Blue (3.3%), and Scottish Fold (2.9%) cats.

Knowledge regarding the epidemiology of neurological diseases in cats is limited; therefore, large-scale data must be studied to enable accurate diagnosis of feline neurological disorders. In this study, we investigated the occurrence of neurological diseases in cats clinically diagnosed at our facility. As a result, our knowledge of the diseases' epidemiology in these animals was expanded, and the diseases' rates, the frequencies of their incidence across cat breeds, and age of onset were obtained. In this survey, there were cases in which the diagnosis was confirmed serologically or histopathologically, as well as cases in which the diagnosis was not confirmed. Therefore, it is necessary to take into consideration that there might be a bias in this survey.

This survey included many crossbred cats (206 animals, 74.6%). Other reports reviewing neurological diseases in cats [1, 8, 12, 17, 19] also predominantly included crossbred cats in the study population. While genetic diseases are frequently found in dogs due to the high number of purebred animals in the population [6, 11], in cats, the incidence of diseases was less influenced by the genetic background. However, the number of purebred cats is thought to be increasing recently in Japan, and we should bear in mind that degenerative, teratogenic, and inflammatory diseases related with genetic anomalies may increase in the future [1, 5, 9, 17].

The lesion distribution in this study was 63.0% in the brain, 17.4% in the spinal cord, and 19.6% in the peripheral neuromuscular system. Although no comparable report has been obtained in cats, previous studies in dogs have found that the incidence of lesions is higher in the spinal cord region than in the brain region compared with this study [6, 11]. This suggests that cats should be

Table 4. Classification of diseases in the peripheral neuromuscular region

	Disease name	Count	Disease rate (%)	Breed of cat	Count	Percentage of cat breed in disease group (%)	Median age (range)
I	FNVNHS	29	82.9	CBC	22	81.5	10 y 2 m (0 y 3 m–16 y)
				Chinchilla	2	7.4	
				Maine Coon	1	3.7	
				Somali	1	3.7	
				Singapura	1	3.7	
Id	IVS	4	11.4	CBC	3	75	5 y 10 m (0 y 7 m–16 y 2 m)
				Persian	1	25	
	PN	2	5.7	CBC	2	100	11 y 10 m (9 y–14 y 7 m)
	Total	35					
Peripheral nerve disease other than head							
DC	PN	10	100	CBC	6	60	4 y 2 m (0 y 5 m–14 y)
				Scottish Fold	2	20	
				Bengal	1	10	
				Munchkin	1	10	
	Total	10					
Myopathy							
M	LPM	1	11.1	CBC	1	100	10 y 8 m
I	PMS	3	33.3	CBC	3	100	0 y 10 m (0 y 4 m–10 y 9 m)
DC	PM	5	55.6	CBC	4	80	10 y 1 m (0 y 4 m–13 y 7 m)
				ASH	1	20	
	Total	9					

M, metabolic disease; I, inflammatory disease; Id, idiopathic disease; DC, difficult to classify; FNVNHS, Facial nerve and vestibular neuropathy, and Horner's syndrome caused by otitis media and otitis externa; IVS, Idiopathic vestibular syndrome; PN, polyneuropathy; LPM, low potassium myopathy; PMS, polymyositis; PM, polymyopathy; CBC, crossbred cats; ASH, American shorthair; y, year; m, month.

considered to have a high morbidity rate in the brain region, unlike dogs.

Regarding disorders in the brain region, the incidence of neoplastic (31.4%) and idiopathic (29.1%) diseases was high. Although the incidence of brain tumors has been reported to be 2.2% [23], this did not include intracranial infiltration of extracranial tumors. For this reason, it seems likely that the rate of tumors causing neurological symptoms in the brain region may be higher, as determined through this survey. In this study, most cases showed meningioma; this was consistent with previous reports [1, 21]. No reports describing the incidence of idiopathic epilepsy (including epilepsy of an unknown origin) in cats could be found, but the incidence was generally considered to be low [16, 20]. For this reason, we need to consider the possibility that idiopathic diseases in the brain area in this study included cases with structural abnormalities that could not be detected through the examinations performed. With regard to inflammatory diseases, infectious encephalitis was diagnosed in all cases in this study; however, in dogs, the incidence of noninfectious encephalitis was considered high [18]. Treatment of noninfectious encephalitis generally includes corticosteroids and/or cyclosporine [18], whereas antibiotics, antifungal agents, etc. are used in cases of infectious encephalitis. Accordingly, there is a difference in the trend of occurrence of inflammatory diseases between dogs and cats, and this should be recognized because it also affects treatment.

In a report summarizing 92 cases of spinal cord disease, the incidence of diseases was 5.4% for degenerative, 3.3% for anomalous, 27.2% for neoplastic, 14.1% for inflammatory, 8.7% for traumatic, and 6.5% for vascular diseases [8]. In another report, summarizing 205 cases of spinal cord disease, the incidence was 6% for degenerative, 1% for metabolic, 27% for neoplastic, 32% for inflammatory, 14% for traumatic, and 9% for vascular diseases [10]. When comparing these with the incidence rates of diseases in the cervical and thoracolumbar spinal cord in this study, the incidence rates of degenerative and vascular diseases in the current study were higher, whereas that of inflammatory diseases was lower than that previously reported [8, 10]. The higher incidence of degenerative diseases is probably due to the larger number of intervertebral disc herniations across all cases than was previously reported. Although in cats the incidence of intervertebral disc herniation is extremely small compared with the incidence in dogs, the reason for this is still unknown. In this survey, the occurrence of vascular diseases was 35.4% combining the cervical cord and thoracic cord regions. The spinal cord infarction, included in vascular diseases, is reported to be unexpectedly high in cats [12]. This likely indicates that spinal cord infarction, a vascular disease, is frequent in cats. Consistent with this survey, previous reports have found that the incidence of spinal cord infarction tended to be higher in the cervical region than in the thoracolumbar region [12, 19]. Because spinal cord infarction is an acute onset disease, it is probably necessary to consider it as a frequent disease in cases where a spinal cord disease in the cervical region is suspected to have developed acutely in a cat. The incidence of inflammatory diseases possibly because cat infectious peritonitis viral meningomyelitis occurred in a low number in this survey compared with that previously reported. The underlying reason for this is probably the small number

of purebred cats in this survey. Meanwhile, infection by feline infectious peritonitis virus is considered to have a high incidence in purebreds [1, 5, 9, 17]. In addition, since not all cases in this survey have been diagnosed histopathologically, the possibility of infection by feline infectious peritonitis virus could not be totally excluded, even if no obvious abnormality was observed with MRI or serological examination [1, 5, 9, 17]. Therefore, the possibility that the actual incidence was higher than that determined through this survey should be taken into consideration.

Diseases in the peripheral neuromuscular region are roughly divided into peripheral nerve diseases, neuromuscular junction diseases, and muscular diseases [2, 22]. The actual incidence of each of these groups of diseases in cats is unknown. In this survey, the incidence of diseases in the peripheral neuromuscular region was 19.6%, which was higher than the 17.4% observed in the spinal cord regions. Therefore, the chances of encountering a peripheral neuromuscular disease in cats may be high. In the diagnostic procedures for peripheral neurological and muscular diseases, it is necessary to consider infections such as *Toxoplasma* [2, 22]. However, serological examinations did not result in any indications for *Toxoplasma* infection in this study. Regarding the causes for peripheral vestibular disease in this survey, otitis media/interna accounted for 82.9% of the head-related peripheral nerve diseases, whereas the cases diagnosed with idiopathic vestibular syndrome accounted for 11.4%. In a retrospective study of vestibular diseases in cats, the incidence of otitis media/interna and idiopathic vestibular syndrome as the cause of peripheral vestibular diseases was equal at 43% [14]. Although the cause for the high incidence of otitis media/interna in this study is unknown, clinicians should be careful not to diagnose the cause of peripheral vestibular disease as idiopathic vestibular syndrome too easily. Ten cases of peripheral nerve diseases related to the limbs and five cases of muscle diseases were difficult to classify because histopathological examination had not been performed. Cases in which symptoms were improved by the administration of corticosteroids were included among the peripheral neurological and muscular diseases difficult to classify other than those of the head. Given this fact, it is likely that diseases difficult to classify contained cases with immune-mediated predisposition.

In order to establish the diagnosis of a neurological disease, in addition to locating the lesions by neurological examination, it is necessary to differentiate diseases by etiological inference. The disease tendencies observed in our survey's results are likely to be useful in these instances. However, to limit the choice of treatment for a disease further, it is necessary to take into consideration the manner of onset and the course after onset [4, 7]. Since the DAMNIT-V disease classification was adopted in this survey, it is possible to ascertain the outline of the manner of onset and the course after onset of each disease. However, although classified into the same DAMNIT-V class, diseases with different modes of onset and/or different courses after onset are included [4]. Therefore, it may be necessary to conduct a detailed survey in which modes of onset, clinical symptoms, etc. are included. This survey summarized Japanese data; hence, disease trends and other trends may have a national and/or regional bias. In addition, because it was a survey conducted at a single facility, we also speculated that bias was introduced to the referred diseases. For these reasons, a larger-scale future survey involving multiple facilities is recommended.

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