An Outbreak of Stringhalt Resembling Australian Stringhalt in Japan

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We report four cases resembling Australian stringhalt observed for the first time in Japan. Between June and July 2000, three of four 4-year-old thoroughbred mares that had been grazed on the same pasture suddenly suffered exaggerated flexion of both hindlimbs. Subsequently, the remaining horse also exhibited mild stringhalt in October. The last horse recovered without treatment one month after occurrence, but the other three horses exhibited severe stringhalt even 5–6 months after occurrence. In one horse, endoscopic examination revealed a left laryngeal hemiplegia. Three of four cases were treated with a combination of drug based treatment (baclofen and phenytoin) and exercise. While phenytoin was effective in treating the stringhalt, the baclofen had no effect. Once the stringhalt improved, treadmill exercise was started to improve hindlimb function. As a result, two of the three horses were able to canter. Three cases underwent electromyography examination and motion analysis. Before treatment, high amplitude electric discharges were observed in the long digital extensor muscle and the lateral digital extensor muscle in the swing and stance phase. The angle of each joint flexed extensively in the swing phase. While Australian stringhalt may heal spontaneously over time, therapy with phenytoin and exercise may hasten a cure.

Key words: *Australian stringhalt, baclofen, electromyography, exercise, phenytoin*

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Stringhalt is a disease in which the tarsal joints of one or both hindlimbs involuntarily show exaggerated flexion during motion. There are two types of this disease, conventional stringhalt and Australian stringhalt [1].

Conventional stringhalt occurs sporadically rather than as an epidemic, with abnormalities recognized in one or both hindlimbs. It occurs regardless of the season and region, and rarely recovers without surgical intervention. On electromyography, abnormal electric discharge is seen in the lateral digital extensor muscle. The cause of the disease is unknown [1].

Australian stringhalt, however, more often occurs in several horses that have grazed on a pasture low in nutrients with many weeds. It tends to cause abnormalities in both hindlimbs, and occurs between

summer and autumn, after the dry season [1, 6]. It is mainly found in Australia [6] and New Zealand [4], but has also been reported in North America [5]. This type of stringhalt reportedly recovers spontaneously within several weeks to ten or more months [6]. In electromyography, abnormalities are observed in the lateral digital extensor muscle, the long digital extensor muscle, and the gastrocnemius muscle [6, 7, 11], as well as a reduction in nerve conduction velocity and tissue abnormalities in the nerves governing these muscles [3, 10]. The cause is assumed ingestion of *Hypochoeris radicata*, or mycotoxins either in the soil or on *Hypochoeris radicata* [6].

We report four cases resembling Australian stringhalt observed for the first time in Japan. We also report case analyses that include treatment results from drugs and exercise, motion analyses and electromyographies of the hindlimbs, upon disease occurrence and after cure.

Symptoms

Between June and July 2000, three of four 4-year-old thoroughbred mares (horses A, B, and C) that had been grazed on the same pasture in Utsunomiya of Tochigi Prefecture in Japan, suddenly suffered exaggerated flexion of both hindlimbs while walking. The affected horses were removed from the pasture and box rested. After these three horses contracted stringhalt, the remaining horse was also box rested and use of the pasture discontinued. Subsequently, the remaining horse (horse D) also exhibited mild stringhalt in October.

The affected horses had been grazed on the pasture for four hours every day since January of the same year, being stabled for the rest of the time. The horses had been undergoing training with no history of lameness before suffering from the disorder. It should be noted that two months prior to onset, all the affected horses had undergone surgery to move the left carotid artery from the carotid sheath to a subcutaneous location. However, four other horses had undergone the same procedure at same time and had been grazed on another pasture without incidence. All horses were fed same feed containing oats, formula feed, and cut hay.

The abnormality was not found in test of hematology (red blood cell, white blood cell, packed cell volume) and serum biochemistry (glutamic oxaloacetic transaminase, creatine kinase, lactate dehydrogenase, blood urea nitrogen).

The severity of stringhalt on onset day of clinical signs, using Huntington's grades [6], was grade III for the horse A (6/19/2000), grade I for horse B (7/26/2000), grade II for horse C (6/7/2000), and grade I for horse D (10/30/2000). The symptoms of stringhalt alternately improved and deteriorated. The horse D recovered without treatment one month after occurrence, but the other three horses, even 5–6 months after occurrence, exhibited severity of grade III to V. There was marked atrophy of hindlimb musculature, particularly at the front of the tibia. Also, in view of reports that laryngeal hemiplegia can occur in conjunction with Australian stringhalt [6], endoscopic examination was conducted, revealing left laryngeal hemiplegia in horse B.

No sign of the disease was seen in about 30 horses that grazed on surrounding pastures. The pasture that may have been the source for stringhalt had been used for grazing for about 30 years, but previously no horse showed symptoms of stringhalt. The conjectured

cause, *Hypochoeris radicata*, could not be found on the pasture or the surrounding pastures. Examination of fungi and mycotoxin was not done, because *Hypochoeris radicata* was not found on the pasture.

Treatment

Five months after occurrence, no improvement was seen in the 3 horses exhibiting severe stringhalt, although horse D recovered spontaneously one month after onset. We used tranquilizer (medetomidine; 3 µg/kg i.v.) in the first place, because excitement exaggerates the stringhalt signs [6]. Hyperflexion with hindlimb was temporarily reduced with tranquilization in one (horse B) of three cases. However, according to disappearance of tranquilization, stringhalt appeared. Therefore, the other drug-based treatment was started (Table 1). The drugs used were the anticonvulsant drug, baclofen^a [9] and the antiepileptic drug, phenytoin^b [7, 9], used previously in the treatment of stringhalt.

Baclofen was administered orally to horse A, at a dosage of 7.1 mg/kg twice a day for one day, 10 mg/kg twice a day for one day, and 10 mg/kg three times a day for eight days. However, no improvement was seen in horse A after 10 days of treatment. Thus, after a 9-day period without drugs, the treatment was changed to phenytoin.

Phenytoin was administered orally to all three horses (A, B, and C), at a dosage of 10 mg/kg twice a day for 14 days. An improvement in stringhalt symptoms was observed after 3 days (horse B) and 8 days (horse A) from the start of phenytoin treatment, with improvement in all horses by the 14th day. To differentiate against improvement from spontaneous recovery, the phenytoin treatment was interrupted for several days, during which time there was an exacerbation of stringhalt symptoms.

Horse C, which had exhibited severe stringhalt, was euthanized 3 days after interruption of the phenytoin treatment and subjected to pathological investigation with a view to clarifying the cause of the disease.

After interrupting phenytoin administration for 6 days, the treatment was resumed for horses A and B, using the same dosage. Phenytoin was mixed directly into the feed in powdered form. Horse A showed no

a: DAINIPPON PHARMACEUTICAL CO., LTD. Osaka, Japan

b: Daiichi Pharmaceutical Co., Ltd. Tokyo, Japan

Table 1. Treatment, symptoms and exercise for three stringhalt horses

Horse A			
day	drug baclofen	sign of stringhalt	exercise
1	14.2 mg/kg/day	grade IV	
2	20 mg/kg/day		
3	30 mg/kg/day		
10	end	grade IV	
cessation period (9 days)			
	phenytoin		
1	20 mg/kg/day	grade IV	
14	end	grade III	
cessation period (6 days)			
21	20 mg/kg/day	grade IV	
43	30 mg/kg/day	grade I (left), grade III (right) grade I (left), grade II (right)	start exercise on treadmill (slope 10%, walk)
69		grade I (left), grade I (right)	(slope 10%, trot)
92		no stringhalt at walk	(slope 5%, canter 7 m/s)
102			(slope 10%, canter 10 m/s)
		grade I (left) at trot grade I at canter	
138	22.5 mg/kg/day		
145	15 mg/kg/day		
152	7.5 mg/kg/day		
160	end	grade I (left) at trot grade I at canter	
176	pathologic autopsy	grade I (left) at trot grade I at canter	
Horse B			
day	drug phenytoin	sign of stringhalt	exercise
1	20 mg/kg/day	grade III	
14	end	grade I	
cessation period (6 days)			
21	20 mg/kg/day	grade I	
29		grade I	start exercise on treadmill (slope 10%, walk)
55		no stringhalt	(slope 10%, canter 8 m/s)
73	15 mg/kg/day		
80	10 mg/kg/day		
87	5 mg/kg/day		
94	end	no stringhalt	
Horse C			
day	drug phenytoin	sign of stringhalt	exercise
1	20 mg/kg/day	grade IV	
14	end	grade III	
17	pathologic autopsy	grade IV	

notable improvement in symptoms after resumption, and continued to exhibit grade II or III stringhalt. Therefore, 43 days after treatment started, the dosage was increased to 15 mg/kg twice a day.

After improvement in the stringhalt symptoms in both horse A and B, treadmill exercise was started to recover hindlimb musculature function, in which some atrophy had been observed. The exercise intensity was

Fig. 1. Change in each joint angle, at a walk, in normal horse and stringhalt horse A, before and after phenytoin treatment. Stick figure represents the calculation of the joint angles of the hindlimb.

increased as the symptoms improved (Table 1). Once cantering was possible, the phenytoin dosage was gradually reduced to zero (Table 1). No recurrence of stringhalt was observed after treatment termination.

Subsequently, to confirm changes in muscle and nerves after improvement in the symptoms, horse A was also euthanized and subjected to pathological investigation. Meanwhile, horse B, still exhibited left laryngeal hemiplegia even after the symptoms had improved.

Motion Analysis

We did motion analysis to observe hindlimb motion changes before and after phenytoin treatment, and to compare affected horses to a normal horse.

Markers were attached to the center of the tuber coxae, hip joint, stifle joint, tarsal joint, and metatarsophalangeal joint on the left side, and each horse's motion was filmed using a high-speed video system (HSV 500C 3)^a at a normal walk at a frequency of 250 Hz. The elements analyzed were the joint angle at the front of the hip joint, stifle joint, tarsal joint, and

fetlock joint, and stick pictures. For the analysis, commercial motion analysis software (Movias for Windows, ver. 1.0)^a was used.

Figure 1 shows changes in joint angles at a walk in horse A, before and after phenytoin treatment, and in a normal horse. The vertical axis shows the angle of each joint. The horizontal axis shows the time standardized by the stride duration (The stride duration is calculated from the beginning of the stance phase to the moment of subsequent landing. One complete stride is expressed as 100% when the time is standardized by the stride duration.). The angle of each joint showed no significant difference compared to a normal horse during the stance phase, but all joints flexed extensively in the swing phase. After the stringhalt was cured by phenytoin treatment, the changes in joint angles were almost same as in the normal horse. The same changes were observed in horse B.

Figure 2 shows stick pictures before and after phenytoin treatment. Before the treatment, all hindlimb joints of all horses flexed excessively at a walk, with the metatarsophalangeal joint raising so much that

a: NAC Image Technology Inc. Tokyo, Japan

Fig. 2. Stick picture in stringhalt horses, at a walk, before and after phenytoin treatment.

it hit the abdomen. After the treatment, however, this exaggerated hindlimb flexion disappeared and normal motion was restored without treatment.

Electromyographies

To observe the state of activity of the hindlimb muscles, electromyographies of the vastus lateralis muscle, the biceps femoris muscle, the semitendinosus muscle, the cranial tibial muscle, the long digital extensor muscle, the lateral digital extensor muscle, the gastrocnemius muscle, and the deep digital flexor muscle were recorded at a walk. For the electrode, Teflon-coated stainless steel wire (Cat. No. 7935)^b was used, inserted into the muscle using a 23G needle. Wires were used as bipolar electrodes and placed at intervals of 3 cm. To record the electromyographies, a 4-channel transmitter (551X)^c was used. The electromyography was amplified 20 times at the transmitter and 50 times at the receiver.

Before the phenytoin treatment, high amplitude electric discharges were observed in the long digital extensor muscle or the lateral digital extensor muscle in the swing phase and the stance phase (Fig. 3). In the vastus lateralis muscle of horse C, moreover, discharges

were stronger than in a normal horse just after ground impact and just before leaving the ground. In the deep digital flexor muscle of horse B, the discharge was divided in the stance. These abnormal discharges were not detected following phenytoin treatment.

Climatic Conditions

Utsunomiya, where the stringhalt occurred, lies about 100 km north of Tokyo on longitude 139° 53'9 E. and latitude 36° 33'10 N, at an altitude of 116.07 m above sea level. The annual average temperature is 13.4°C, and the annual average precipitation 1,443.4 mm. Table 2^d compares the monthly precipitation and average temperature in 2000, when the disease broke out, with the monthly precipitation and average temperature in 1971–2000. Precipitation in the period before the outbreak was lower than the average annual value in February, however, in April, it was higher than average. The monthly average temperature in 2000 showed no significant deviation from other years.

b: A-M Systems, Inc. Carlsborg, WA

c: NEC San-ei Instruments, Ltd. Tokyo, Japan

d: Utsunomiya Local Meteorological Observatory

Fig. 3. Electromyography in normal horse and stringhalt horse, at a walk before phenytoin treatment. Calibration bar: horizontal axis 0.5 s, vertical axis 0.75 mV.

Table 2. Comparison of monthly precipitation and average temperature in the year stringhalt occurred (2000) and 1971–2000

	precipitation (mm)		average temperature (°C)	
	2000	1971–2000	2000	1971–2000
Jan.	52.0	26.8	4.5	2.1
Feb.	10.0	46.9	2.6	2.8
Mar.	60.0	81.5	6.5	6.2
Apr.	178.5	119.3	12.1	12.1
May	152.0	144.1	18.0	16.8
Jun.	174.0	193.6	21.2	20.3
Jul.	276.5	183.9	25.7	23.8
Aug.	195.5	201.0	26.2	25.3
Sep.	327.5	234.5	23.0	21.4
Oct.	125.5	120.1	16.4	15.7
Nov.	79.0	66.3	10.3	9.7
Dec.	3.0	25.5	4.6	4.4

Discussion

The outbreak of stringhalt reported here showed some points of divergence from Australian stringhalt. However, the fact that stringhalt was contracted by all four horses that had been grazed on the same pasture suggests that, like Australian stringhalt, the ingestion of some substance on the pasture led to the outbreak.

The differences between the stringhalt we experienced and Australian stringhalt were the season of the outbreak and the absence of *Hypochoeris radicata*. Australian stringhalt usually occurs in late summer or autumn after the dry season [6]. This outbreak, however, occurred between June and July in early to midsummer, which is the rainy season in Japan. Moreover, the precipitation before the outbreak was higher than normal. This concurs with the report by

Gay *et al.* [5] on symptoms similar to Australian stringhalt in the Northern Hemisphere, in that there was no dry season before the outbreak. However, their outbreak occurred in late summer, different from the timing in the present report. On the other hand, June and July, when our stringhalt occurred, is the flowering season of *Hypochoeris radicata* in Japan. This agrees with a previous report in which Australian stringhalt occurred in the flowering season [6].

The presence of *Hypochoeris radicata*, could not be confirmed in our pasture. However, *Hypochoeris radicata* is a naturalized plant native to Europe, and first appeared in Japan about 60 years ago. Today, it is widely found in Japan, particularly in Hokkaido. These facts suggest that, although we could not find *Hypochoeris radicata* in the pasture, a few might have existed in the pasture. However, there is little possibility that the affected horses ate a large quantity of *Hypochoeris radicata*.

Nevertheless, no outbreak was observed in groups of horses fed identical feed, all four horses that grazed on the same area of pasture exhibited stringhalt. This leads to the conclusion that the ingestion of some substance on the pasture led to the outbreak.

Points in common with Australian stringhalt were that the stringhalt was observed in both hindlimbs, and that it was accompanied by laryngeal hemiplegia. Australian stringhalt recovers spontaneously within several weeks to several months [6]. The horse D recovered without treatment one month after occurrence. Thus, although this outbreak differed from Australian stringhalt in some respects, the manifested symptoms resembled those of Australian stringhalt, leading us to consider a common cause might be involved.

While phenytoin was effective in treating the stringhalt reported here, baclofen had no effect. Phenytoin stabilizes nerve cell membranes, suppresses the augmentation effect in the synapse, and contains the spread of excitation in the central nervous system [8]. It is considered effective against major epilepsy. Baclofen, on the other hand, is an aminobutyric acid (GABA) derivative, and suppresses both mono- and polysynaptic reflexes in the spinal cord and reduces the activity of γ motor neurons. It is used to treat spastic paralysis such as infant cerebral paralysis or post-traumatic spinal cord damage [2]. The effectiveness of these two drugs in treating stringhalt differs since their mechanisms and their effects differ.

In addition to stabilizing nerve cell membranes,

phenytoin has a sedative side effect. The symptoms of stringhalt worsen if a horse is excited [7], and tranquillizer temporarily reduced the sign of stringhalt. Some reports suggest the sedative effect of phenytoin plays a part in improving these symptoms [7]. However, no sedative effect was observed in the three horses treated this time.

Reports suggest that Australian stringhalt recovers spontaneously, from several weeks to several months after occurrence [6]. We discontinued phenytoin for 6 days to discern if symptom improvement was due to spontaneous healing or the effect of the drug. However, the stringhalt symptoms intensified after the interruption, suggesting improvement was due to the phenytoin.

Phenytoin was administered to horse A for 160 days and horse B for 94 days. But despite such long treatment periods, no side effects were observed.

Once the stringhalt symptoms improved with phenytoin treatment, treadmill exercise was started. The symptoms improved further due to the exercise, and exercise intensity was gradually increased as symptoms improved. As a result, the horses resumed their full range of gaits, including canter, and no recurrence of stringhalt was observed even after discontinuing the phenytoin. Therefore, combining phenytoin administration with exercise might be effective for improving symptoms and recovering normal hindlimb motion.

Hindlimb motion analysis showed exaggerated flexion of various joints in the swing phase. Abnormal electromyographies of the lateral digital extensor muscle and long digital extensor muscle are observed in horses suffering from stringhalt [7], and our observations confirmed those findings. However, even if only the lateral digital extensor muscle and long digital extensor muscle contracted abnormally, considering the function of these muscles, this would cause flexion of the tarsal joint and extension of the metatarsophalangeal joint. Therefore, exaggerated flexion in all hindlimb joints would not be expected. In our cases, abnormal discharge was also observed immediately before leaving the ground in the vastus lateralis. This suggested that abnormalities also occurred in other nerves and muscles besides the lateral digital extensor muscle and long digital extensor muscle, or that other non-affected muscles acted with abnormal timing to compensate abnormal action of these muscles.

To date, there are no reports in Japan of stringhalt

similar to Australian stringhalt, affecting both hindlimbs and occurring in groups that graze on the same pasture. Although it was not possible to identify the cause of the stringhalt in the present report, Australian stringhalt may also occur in Japan in future, owing to the wide distribution of *Hypochoeris radicata* in Japan.

While Australian stringhalt may heal spontaneously after some months, treatment with phenytoin and exercise may reduce the period until cure. The lateral digital extensor muscle and long digital extensor muscle, in which electromyographic abnormalities were observed, had already atrophied because treatment was started 5 or 6 months after occurrence. However, if treatment were started earlier, i.e. before the occurrence of atrophy, it may be possible to reduce the treatment period, because motoneuron disorder might be involved in this stringhalt.

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