Factor for Diagnosis Delay on Symptomatic Dural Arteriovenous Fistula in Central Nervous Systems

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Objective: Symptomatic dural arteriovenous fistula (sDAVF) has various manifestations. As patients with sDAVF consult specialists on the basis of the symptoms they are experiencing, there is a possibility that diagnosis could be delayed if the specialists are not neurologists. We investigated the medical history of sDAVF patients and the time interval from onset to hospitalization, MRI and diagnosis, in order to clarify the diagnostic delay in such patients.

Methods: We defined each stage from sDAVF onset to diagnosis as follows: day of onset (Sx), day of first visit to doctor $(1^{st} Dr)$, day of second visit to doctor $(2^{nd} Dr)$, total number of doctors (relay), day of initial MRI study $(1^{st} MR)$, and day of diagnosis (Dx). We then calculated the time interval in days between each stage as: (Sx-Dx), (Sx-1st Dr), $(1^{st} Dr-1^{st} MR)$, and $(1^{st} MR-Dx)$. We divided the 20 patients into two groups according to the period from onset to diagnosis: a "no delay" group of less than 70 days, and a "delay" group of more than 71 days, and analyzed which specific time interval was mostly responsible for the delay in sDAVF diagnosis.

Results: There was significant differences between the two groups in time intervals $(1^{st}Dr-1^{st}MR)$ (5.5days vs 83 days, p = 0.0043) and in numbers of relay (2.5 vs 4, p = 0.0211). Whereas no influence in time intervals of (Sx-1stDr) (6.5 days vs 30.5 days, p = 0.3288) and $(1^{st}MR-Dx)$ (2.5days vs 14 days, p = 0.206).

Conclusion: Undertaking an MRI study was most important factor for sDAVF diagnosis. Increased awareness of this disease might shorten the (1st Dr-MR) time

interval and facilitate speedier and more accurate diagnosis.

Key words: dural arteriovenous fistula

INTRODUCTION

A symptomatic dural arteriovenous fistula (sDAVF) manifests with a variety of clinical symptoms, such as eye symptoms, tinnitus, headaches, and unspecified neurological symptoms [1]. As such, patients rely on their subjective symptoms and consult with not only neurosurgeons (NS), but also physicians in different departments, such as neurologists (N), ophthalmologists (Oph), otolaryngologists (Oto), orthopedists (Orth), and general physicians (GP). However, since this condition is not well known by physicians other than NS, in many cases, it could take numerous consultation days to establish a diagnosis after the onset of symptoms. Since DAVF patients with retrograde cortical venous reflux (RCVR) are at risk of developing intracranial hemorrhage and cerebral venous infarction [2-6], it is imperative to avoid delays in diagnosis.

Magnetic resonance imaging (MRI) is essential for identifying clues for diagnosing this condition, and cerebral angiography (CAG) is often necessary to confirm the diagnosis.

Using data of sDAVF patients who underwent surgical interventions at our hospital, the stages of the medical consultation process that are involved from the onset of sDAVF to a definitive diagnosis within our hospital's medical district were analyzed. To identify the factors affecting the time lag to reach a definitive diagnosis, the number of days until a definitive diagnosis was established was retrospectively investigated, and the rate-limiting stages of the medical consultation process were analyzed.

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SUBJECTS AND METHODS

Subjects

Shimane Prefecture is located on the western side of Honshu island in Japan, with an area of 6707 km² and a population of approximately 680,000 people. It is a region with a high proportion of elderly people, with 33.6% of the population being 65 years or older. There is no heavy manufacturing industry in the region, and the demographic statistics are relatively stable. There are 1947 physicians (1534 in the Eastern region and 413 in the Western region), and while there is an uneven distribution of doctors, there are 279 physicians per 100,000 population throughout the entire prefecture. Compared to the national average (244.9 physicians/100,000 population), it is a prefecture with sufficient physicians. In the entire prefecture, there are 51 hospitals with inpatient facilities that offer 20 or more hospital beds, with a total of 31 MRI units. Our medical facility functions as a base hospital in Shimane Prefecture, and patients are referred to our facility from all over the prefecture.

The study period was from January 2004 to March 2018 (14 years and two months). Of the 27 consecutive DAVF patients who were hospitalized at our medical facility during the study period, 20 patients with sDAVF were selected for the present analysis.

Methods

The following parameters were examined: age at treatment, sex, clinical symptoms, shunt location, presence or absence of RCVR, specialty of the consulting physician, medical district of the consulting physician, day of symptom onset (Sx), day of first consultation (1stDr), day of referral to a secondary medical institution (2ndDr), number of transferred medical institutions (Relay), day of first MRI test (1stMR), day of first CAG (1stAngio), and day of definitive diagnosis (Dx) (Fig. 1).

The clinical symptoms were classified into the following: eye symptoms (Eye symptoms), ear symptoms (Ear symptoms), headaches (HA symptoms), cranial nerve symptoms (CNs symptoms and spinal nerve symptoms (Spine symptoms). Eye symptoms consisted of injected conjunctiva, edema, and ocular proptosis. Ear symptoms consisted of tinnitus, vascular bruit, equilibrium disorder, and unsteadiness. HA symptoms were head pain and heaviness of the head. Cranial symptoms consisted of cranial nerve palsies, higher brain dysfunction, cerebral ischemia, cerebral hemorrhage, loss of consciousness, and convulsions. Spine symptoms consisted of four-limb paresthesiae and muscular weakness.

The location of the DAVF was confirmed angiographically, and it was classified as follows: cavernous sinus (CS), transverse-sigmoid sinus (TS-SS), tentorial (Tent) and spinal (Spine).

The specialization of the consulting physicians was as: NS, N, Oph, Oto, Orth, and GP.

Based on the number of physicians per 100,000 population, the medical districts in Shimane Prefecture that the consulting physicians worked at were grouped into medically adequately served (MAS) areas and medically underserved (MU) areas. The number of physicians in each medical district was obtained from the December 2016 medical statistics of Shimane Prefecture. The number of physicians per 100,000 population was as follows: 455.2 in Izumo district, 262.8 in Matsue district, 223.7 in Hamada district, 197.3 in Masuda district, 182.1 in Ooda district, and 131.2 in Unnan district. Based on the number of physicians per 100,000 population, the medical districts of the consulting doctors were defined as follows: i) MAS areas: Izumo, Matsue, and Hamada districts (population: 500,333; number of physicians: 1610; number of physicians per 100,000 population: 321.8); and ii) MU areas: Masuda, Ooda, and Unnan districts (population: 175,722; number of physicians: 302; number of physicians per 100,000 population: 171.9) (Fig. 2). The number of MRI units in each medical district was as follows: 22 units in the MAS areas (4.40 MRI units per 100,000 population); and nine units in the MU areas (5.12 units per 100,000 population). The number of specialized NS in each medical district was as follows: 31 NS in the MAS areas (6.20 NS per 100,00 population); and five NS in the MU areas (2.85 NS per 100,00 population) (Table 1).

The following definitions were used to describe the days that elapsed at each stage of the medical consultation process from sDAVF onset to defini-



Fig. 1. Parameters examined

Clinical symptoms, shunt location, presence or absence of RCVR, specialization of the consulting physician, medical district of the consulting physician, Sx, 1stDr, 2ndDr, 1stMR, and Dx were examined, and the number of days at each stage of the medical consultation process were calculated.

Table 1. Comparison of MAS and MU areas in Shimane Prefecture

Medical area	Adequately served area	Underserved area	all japan
Medical alea	matue, izumo, hamada	unnan, ooda,masuda	2014
Number of medical doctors	1610	302	
Number of medical doctors per 100,000 population	321.8	171.9	222
Number of MRI machines	22	9	
Number of MRI machines per 100,000 population	4.4	5.12	4.2
Number of neurosurgical specialists	31	5	
Number of neurosurgical specialists per 100,000 population	6.2	2.85	5.4

The number of physicians per 100,000 population based on the total population of Japan in 2014, number of MRI units, and the number of specialized NS are compared in the MAS areas (Izumo, Matsue, and Hamada districts) and MU areas (Masuda, Ooda, and Unnan districts) in Shimane Prefecture.



Fig. 2. Medical districts in Shimane Prefecture

The medical districts in Shimane Prefecture are divided into six districts. Based on the number of physicians per 100,000 population, the MAS areas (Izumo, Matsue, and Hamada districts) are shown in dot, and the MU areas (Masuda, Ooda, and Unnan districts) are shown in white. tive diagnosis: Sx, the day a patient experienced a clinical symptom related to DAVF; 1stDr, the day of first visit at any type of medical institution since experiencing a symptom related to DAVF; 2ndDr, the day a patient visited a secondary medical institution after a referral by the first consulting physician; 1st MR, first MRI following the onset of the symptom; Dx, the day a definitive diagnosis of DAVF was established (the day DAVF was diagnosed using MRI or the day DAVF was diagnosed using CAG because the MRI was inconclusive).

The number of transferred medical institutions (Relay) refers to the number of visited medical institutions between the first consultation physician and our Neurosurgery Department.

Analytical methods

The number of consultation days was tabulated as an analytical parameter (Fig. 1).

- (1)Days (Sx-Dx): Number of days between Sx and Dx
- (2) Days (Sx-1stDr): Number of days between Sx and $1^{st}Dr$
- (3) Days $(1^{st}Dr-2^{nd}Dr)$: Number of days between $1^{st}Dr$ and $2^{nd}Dr$
- (4) Days $(1^{st}Dr-1^{st}MR)$: Number of days between $1^{st}Dr$ and $1^{st}MR$
- (5) Days (1stMR-Dx): Number of days between $1^{st}MR$ and Dx

Definition of delayed diagnosis

When the Days (Sx-Dx) were calculated for the 20 sDAVF patients, the median duration to definitive diagnosis was 70 days. The present study used 70 days as the benchmark, which was the median duration to establish a definitive diagnosis, and the subjects were divided into two groups. The normal diagnosis group consisted of patients who were diagnosed within 70 days. The delayed diagnosis group consisted of patients who were diagnosed after 71 days.

Statistics

Statistical analysis used descriptive statistics and estimated processing. The sample size (n) and median values were calculated using descriptive statistics. The data were tabulated in Excel and analyzed with JMP ver.9.0.0. Since the data for the present study did not show a normal distribution or homoscedasticity, non-parametric estimation procedures were used. For n-values of two or less, the actual values were used instead of the estimate.

The Mann-Whitney-Wilcoxon (MWW) test was used to compare continuous variables between two groups. Significance was set at p = 0.05. Confounding factors were evaluated when significance was observed between two groups, and highly independent factors were identified. After the crosstabulation of nominal variables, Fisher's exact test was used, and significance was set at p = 0.05. Moreover, since a degree of expectation less than five cells could not be tested, it was reported as not tested (NT).

RESULTS

Breakdown of sDAVF, department of first consultation, and medical districts

During the study period, 20 patients received sDAVF treatment at our medical facility. There were 12 men and 8 women, with a mean age of 70.5 years (range, 55-81 years).

The primary symptoms were as follows: Eye symptoms (7), Ear symptoms (5), HA symptoms (4), Cranial symptoms (2), and Spine symptoms (2).

The shunt locations were CS (8), TS-SS (7), Tent (3), and Spine (2).

The specializations of the physicians where the patients first consulted were as follows: NS (3), N (2), Oph (7), and GP (8). None of the patients went for their initial consultation to Orth or Oto (Table 2).

Days from onset to the first consultation, first MRI, and each stage of the medical consultation process to reach definitive diagnosis

Table 3 shows the median days of each stage of the medical consultation process before the DAVF diagnosis was made in the 20 subjects. The median Days (Sx-Dx) was 70 days (between 0 and 3659 days). The median Days (Sx-1stDr) was 6.5 days (between 0 and 1713 days). The median Days $(1^{st}Dr-2^{nd}Dr)$ was 19.5 days (between 0 and 1146

Sx-Dx tim	e	Total $(n = 20)$	no delay group (n = 10)	delay group (n = 10)	<i>p</i> -value
Age	median	70.5	70.5	70	0.9396(MUW test)
Sex	male	12	7	5	0.6499((Fisher test: 2-side)
	female	8	3	5	0.0499((11sher test. 2-side)
	Eye	7	3	4	
	Ear	5	3	2	
Symptoms	HA	4	2	2	NT
	Cranial	2	2	0	
	Spinal	2	0	2	
	CS	8	3	5	
Shunt site	TS-SS	7	4	3	NT
	Tent	3	3	0	19.1
	Spine	2	0	2	
	NS	3	3	0	
	Ν	2	2	0	
Department of 1st Dr	Oph	7	3	4	NT
	Oto	0	0	0	IN I
	Orth	0	0	0	
	GP	8	2	6	

Table 2. Background characteristics of the normal and delayed diagnosis groups

Days (Sx-Dx) are separated into the normal diagnosis group (70 days or less) and the delayed diagnosis group (71 days and over). The age, sex, symptoms, shunt position, and specialization of the physician at the first consultation for the two groups are shown.

Table 3. Comparison of days between the normal and delayed diagnosis groups for each stage

Sx-Dx time	;	Total $(n = 20)$	no delay group $(n = 10)$	delay group (n = 10)	<i>p</i> -value (MUW test)
Days(Sx-DX)	median	70	28	178.5	0.0002
Days(Sx-1st Dr)	median	6.5	6.5	30.5	0.3288
Days(1st Dr-2nd Dr)	median	19.5	14.5	82.5	0.021
Days(1st Dr-1st MR)	median	14	5.5	83	0.0043
Days(1st MR-Dx)	median	3.5	2.5	14	0.206
relay	median	3	2.5	4	0.0211

The number of elapsed days to reach a definitive diagnosis from each of the stages of the medical consultation process for the two groups is compared. A significant difference is observed in Days $(1^{st}Dr-1^{st}MR)$, Days $(1^{st}Dr-2^{nd}Dr)$, and the number of transferred medical institutions from the first consultation to our Neurosurgery Department (Relay).

days). The median Days (1stDr-1stMR) was 14 days (between 0 and 481 days). The median Days (1stMR-Dx) was 3.5 days (between 0 and 2641 days).

Comparison between the normal and delayed diagnosis groups

The numbers of elapsed days from onset to the first consultation, first MRI, and each stage of the medical consultation process to reach a definitive diagnosis were analyzed between the normal and delayed diagnosis groups using the MWW test (Table 3).

The median number of days between the various medical consultation stages for the normal and delayed diagnosis groups are noted below. Days (Sx-Dx): normal diagnosis group (28 days); delayed diagnosis group (178.5 days)

Days (Sx-1stDr): normal diagnosis group (6.5 days); delayed diagnosis group (30.5 days)

Days (1stDr-2ndDr): normal diagnosis group (14.5 days); delayed diagnosis group (82.5 days)

Days (1stDr-1stMR): normal diagnosis group (5.5 days); delayed diagnosis group (83 days)

Days (1stMR-Dx): normal diagnosis group (2.5 days); delayed diagnosis group (14 days)

The P values between the two groups for each of the periods were Days (Sx-Dx): 0.0002; Days $(Sx-1^{st}Dr)$: 0.3288; Days $(1^{st}Dr-2^{nd}Dr)$: 0.021; Days $(1^{st}Dr-1^{st}MR)$: 0.0043; and Days $(1^{st}MR-Dx)$: 0.206.

Of the various stages of the medical consultation

process, a significant difference between the two groups was observed in Days (1stDr-1stMR) and Days (1stDr-2ndDr) before a DAVF diagnosis was reached. On the other hand, there was no significant difference between the two groups for Days (Sx-1stDr) and Days (1stMR-Dx). The first MRI led to a diagnosis in 14 of the 20 patients, six patients required additional MRI, and two patients needed CAG.

As for the number of transferred medical institutions from the first consultation to our Neurosurgery Department (Relay), there was a significant difference (p = 0.0211) between the normal diagnosis group (2.5) and the delayed diagnosis group (4). The specialization of the first consulting physician was as follows: normal diagnosis group (NS = 3; N = 2; Oph = 3; GP = 2) and delayed diagnosis group (NS = 0; N = 0; Oph = 4; GP = 6). Since 5 of 10 patients in the normal diagnosis group first consulted with either an NS or N, they tended to visit fewer medical institutions before a diagnosis was made.

Primary symptoms and the number of days to each stage of the medical consultation process

The median number of days to reach each medical consultation stage was calculated for each primary symptom. The Days (Sx-Dx) for each symptom were: Eye symptoms (118 days), Ear symptoms (45 days), HA symptoms (115 days), Cranial symptoms (12.5 days), and Spine symptoms (956.5 days). Cranial symptoms were diagnosed the earliest.

The Days (Sx-1stDr) for each symptom were: Eye symptoms (25 days), Ear symptoms (12 days), HA symptoms (0.5 days), Cranial symptoms (0 days), and Spine symptoms (917.5 days). While patients immediately visited a medical institution after experiencing any type of headache, for Spine symptoms, it took some time before patients first consulted a medical institution.

The Days (1stDr-1stMR) for each symptom were: Eye symptoms (33 days), Ear symptoms (7 days), HA symptoms (77 days), Cranial symptoms (0 days), and Spine symptoms (25 days). There was a time lag before MRI was performed for Eye, HA and Spine symptoms.

The following were the Days $(1^{st}MR-Dx)$ for

each symptom: Eye symptoms (0 days), Ear symptoms (15 days), HA symptoms (24.5 days), Cranial symptoms (12.5 days) and Spine symptoms (14 days). No significant difference was observed in the number of days to reach a diagnosis.

Effects of RCVR

An examination was undertaken to determine whether there was a difference in consultation days between the presence or absence of RCVR. Of the 20 subjects, 11 patients were RCVR-positive, and seven patients were RCVR-negative. Two patients were excluded from the analysis because they had spinal DAVF.

RCVR-positive patients had the following symptoms: Eye symptoms (4), Ear symptoms (2), HA symptoms (3), and Cranial symptoms (2). The symptoms for the RCVR-negative patients were: Eye symptoms (3), Ear symptoms (3), HA symptoms (1) and Cranial symptoms (0).

The specializations of the first consulting physician in the RCVR-positive patient group were NS (2), N (1), Oph (4), and GP (4). For the RCVRnegative patient group, the specializations were NS (1), N (1), Oph (3), and GP (2).

Statistical analysis was not performed due to the small sample size. While many RCVR-positive patients tended to have HA and Cranial symptoms, they were not inclined to consult an NS or N.

The median Days (Sx-1stDr) was 0 days for the RCVR-positive patients and 34 days for the RCVR-negative patients (p = 0.0202). The median Days (Sx-Dx) was 34 days for RCVR-positive patients and 69 days for RCVR-negative patients (p = 0.7511). Patients with RCVR consulted a medical institution at a significantly earlier stage (Table 4).

Sub-analysis of Eye symptoms

Transferred medical institutions, specialization of the consulting physician, affiliated medical districts, and the number of consultation days from the 1stDr to Dx were examined in the seven patients with Eye symptoms. The patients visited between two to five medical institutions before reaching a definitive diagnosis, and the seven patients with Eye symptoms targeted in the present analysis consulted with 21 physicians [N (2), NS (4), Oph (14), and GP

Retrograde cortical venous	reflux(RCVR)	positive $(n = 11)$	negative $(n = 7)$	<i>p</i> - value M-W test
Symptoms	Eye	4	3	
	Ear	2	3	NT
	HA	3	1	NT
	Cranial	2	0	
Department of 1st Dr	Ns	2	1	
	Ν	1	1	NT
	Oph	4	3	18.1
	GP	4	2	
Days(Sx-1st Dr)	median	0	34	0.0202
Days(Sx-Dx)	median	34	69	0.7511

TAULE 4. EXAMINATION OF NUMBER	Table 4.	Examination	of RCVR
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An examination was undertaken to determine whether there was a difference in the number of consultation days between the presence and absence of RCVR. More RCVR-positive patients tended to have HA and Cranial symptoms; however, they were not inclined to consult NS or N. The median Days (Sx-1stDr) for RCVR-positive patients are 0 days compared to 34 days for RCVR-negative patients (p = 0.0202). This means that there is a significant difference, and patients with RCVR consulted medical institutions at an earlier stage.



Fig. 3. Examination of patients with Eye symptoms

The transferred medical institutions, specialization of the consulting physician, affiliated medical districts, and consultation days from 1stDr to Dx are examined.

(1)]. The mean number of consultation days for each physician was 37.5 days (between 0 and 273 days) (Fig. 3). The number of consulting physicians and the mean number of consultation days for each physician was calculated for MAS and MU areas. For MAS areas, there were 14 consulting physicians, and the mean number of consultation days was 14.1 days (between 0 and 147 days). In the MU areas, there were seven consulting physicians, and the mean number of consultation days was 84.4 days (between 0 and 273 days) (p = 0.0015) (Table 5).

Since the patients with Eye symptoms were aware of their own eye abnormalities, such as injected conjunctiva, edema, and ocular proptosis, 14 of the 21 physicians that they visited were Oph.

Medical area	all doctor	medical duration per one doctor		
Wiedlear area	(n)	(mean days)		
Izumo	11	16.7		
Matsue	-	-		
Hamada	3	4.3		
Adequately served area	14	14.1		
Masuda	3	49		
Ooda	3	143.3		
Unnan	1	14		
Underserved area	7	84.4		

Table 5. Examination of patients with Eye symptoms: Mean number of consultation days per physician in each medical district

There is a significant difference (p = 0.0015) in the mean number of consultation days per physician between MAS areas (14.1 days) and MU areas (84.4 days).

 Table 6. Examination of patients with Eye symptoms: Mean number of consultation days per

 Oph for each medical district

Medical area	ophthalmologist	medical duration per one doctor		
	(n)	(mean days)		
Izumo	7	23		
Matsue	-	-		
Hamada	2	5.5		
Adequately served area	9	19.1		
Masuda	2	73.5		
Ooda	2	167		
Unnan	1	14		
Underserved area	5	99		

There is a significant difference (p = 0.0125) in the mean number of consultation days per Oph between MAS areas (19.1 days) and MU areas (99.0 days).

The number of Oph and the mean number of consultation days for each Oph between the MAS and MU areas were calculated, focusing only on the Oph that examined the Eye symptom patients. In the MAS areas, there were nine Oph, and the mean number of consultation days was 19.1 days (between 0 and 147 days). In the MU areas, there were five Oph, and the mean number of consultation days was 99.0 days (between 0 and 273 days) (p = 0.0125) (Table 6).

DISCUSSION

The importance of MRI for the diagnosis of sDAVF

The present study retrospectively investigated the length of time that elapsed from onset to definitive

diagnosis [Days (Sx-Dx)] of all types of DAVF. The normal and delayed diagnosis groups were divided based on the Days (Sx-Dx) to determine which stage of the medical consultation process was related to the delay in diagnosing DAVF. The statistical analysis showed that there was a significant difference (p = 0.0043) in the Days (1stDr-1stMR) between the normal diagnosis group (5.5 days) and the delayed diagnosis group (83 days). There was also a significant difference (p = 0.021) in Days (1stDr-2ndDr) between the normal diagnosis group (14.5 days) and the delayed diagnosis group (82.5 days). There was no significant difference in Days (Sx-1stDr) and Days (1stMR-Dx).

As for the number of transferred medical institutions from the first consulting physician to our Neurosurgery Department (Relay), there was a significant difference (p = 0.0211) between the normal diagnosis group (2.5) and the delayed diagnosis group (4). While a statistical analysis was not possible due to the limited sample size, the specialization of the first consulting physician for 5 of the 10 patients in the normal diagnosis group was either neurosurgery or neurology. Compared to the delayed diagnosis group, the normal diagnosis group had an MRI at an earlier stage and tended to have been transferred to fewer medical institutions before reaching a definitive diagnosis.

According to the analysis of the above results, the stage of the medical consultation process that affects the delay in diagnosing sDAVF, the rate-limiting stage, is not determined by how fast a patient consults a medical institution, but it is mostly influenced by how early a physician performs MRI, and also by how fast the first consulting physician refers the patient to a secondary medical institution.

Studies on the time lag between DAVF onset and diagnosis have focused on spinal DAVF [7, 8]; however, according to our extensive literature search, no previous studies have investigated the period between onset and diagnosis of all types of sDAVF including cranial DAVF, making this the first study of its kind.

In spinal DAVF, overlooking the MRI test results and misdiagnosis tended to delay the diagnosis [7, 8]. In the present study, the diagnostic rate with the first MRI was 14 of 20 (60%). Even though images could not be equalized since they were not taken by the same imaging unit, the results still reflected the difficulty in MRI diagnosis of DAVF. While there was no significant difference in Days (1stMR-Dx) between the normal diagnosis group (2.5 days) and the delayed diagnosis group (14 days), the impression was that there was a slight delay in the delayed diagnosis group. There were three patients in the normal diagnosis group and three patients in the delayed diagnosis group who were not diagnosed during the first MRI and required either additional MRI or CAG. Factors that affected Days (1stMR-Dx) were not only the accuracy of MRI, but also the number of days required to establish cooperation between hospitals. In the delayed diagnosis group, there was a patient that required some time in establishing cooperation between hospitals, and that may have influenced the Days $(1^{st}MR-Dx)$ of the delayed diagnosis group.

Issues related to early diagnosis of DAVF

For early diagnosis of DAVF, in other words, to shorten Days (Sx-Dx) of DAVF, the most important issue is to shorten Days $(1^{st}Dr-1^{st}MR)$.

Cavernous sinus is the most common location of DAVF but DAVF has a variety of clinical symptoms depending on the shunt location, departments other than the specialized neurosurgery department often become involved. When the Days (Sx-Dx) according to different clinical symptoms was investigated in the present study, the median number of days for patients with Cranial symptoms was five days, and it was diagnosed the fastest. This was because NS or N examined the patients during the first consultation, and with central neurological diseases in mind, they requested head MRI at an early stage. In contrast, the median Days (Sx-Dx) for patients with Eye and HA symptoms were 118 and 115 days, respectively, since these patients tended to receive symptomatic treatment for a certain amount of time at the ophthalmology or general practice department. The median Days (Sx-Dx) for patients with spinal symptoms was 965 days, an extremely long time. The prolonged time lag between Sx and the 1stDr was due to the slow-progressive nature of vesicorectal disorders and ambulatory dysfunctions, which tended to result in a long time between onset and definitive diagnosis. As noted above, DAVF is a condition that is not well known by physicians who are not specialized in neurological disorders, and symptomatic treatments tend to be continued without suspecting central neurological diseases. When examining RCVR cases, patients with RCVR tended not to consult with NS or N during their first consultation. This meant that patients with a high risk of cerebral hemorrhage were in danger of being followed-up in departments that do not specialize in neurological disorders.

Next, seven patients with Eye symptoms were sub-analyzed (Fig. 3). There was an uneven distribution of physicians in Shimane Prefecture, and the number of physicians per 100,000 population in MAS areas (Izumo, Matsue and Hamada districts) was 321.8 physicians, and in MU areas (Masuda, Ooda, and Unnan districts) it was 171.9 physicians. An investigation was undertaken to determine whether there was a difference in the mean number of consultation days per physician that examined patients with Eye symptoms between MAS and MU areas. There was a significant difference (p = 0.015) between MAS areas (14.1 days; between 0 and 147) and MU areas (84.4 days; between 0 and 273 days) (Table 5). Even when the investigation was limited to Oph, there was a significant difference (p= 0.0125) between MAS areas (19.1 days; between 0 and 147 days) and MU areas (99.0 days; between 0 and 273 days) when the mean number of consultation days per Oph examining patients with Eye symptoms was calculated (Fig. 3).

In patients with Eye symptoms, both the patients and physicians clearly recognized the Eye symptoms, yet in MU areas, it required a significantly longer period to establish a diagnosis. In MU areas, significantly longer consultation days were required, even for physicians specializing in ophthalmology. There was a pronounced tendency of patients being transferred from one Oph to another, with the transferred medical institutions not being able to narrow down the diagnosis. Since this condition is not well known by physicians other than NS, in many cases, it could take numerous consultation days to establish a diagnosis after the onset of symptoms. However, these results may be proof of a consultation process that occurred difference of DAVF cognitions between doctors of MAS areas and doctors of MU areas.

When discussing inequalities in healthcare access between the MAS and MU areas, it is essential to consider not only the number of physicians per 100,000 population, but also the number of operational MRI units and the number of specialized NS. In the MAS and MU areas, there were 22 and 9 operational MRI units, respectively. This corresponds to 4.40 operational MRI units in the MAS areas and 5.12 units in the MU areas per 100,000 population. In other words, there were more units in MU areas. However, people living in MU areas face difficult conditions in accessing hospitals with MRI units due to geographical barriers and inadequate means of transportation, and, therefore, consulting physicians are in an environment where they cannot readily order MRI.

An important factor is also the availability of a medical environment that is easy for GP, Oph, and Oto to refer patients suspected of DAVF to NS. The number of specialized NS in the MAS and MU areas was 31 and 5, respectively. When these figures are shown per 100,000 population, there was a marked significant difference between the number of specialized NS in MAS (6.20) and MU (2.85) areas. Thus, the number of NS in MU areas may be affecting the delay in diagnosis in MU areas. Obviously, it is important for physicians, such as GP and Oph, who are not specialized in neurology to collaborate with NS in MU areas. However, there is also a need to create an environment where suspected DAVF patients can be easily referred to NS in base hospitals such as ours by physicians in MU areas that are not specialized in neurological conditions.

Delay in diagnosing DAVF could lead to intracranial hemorrhage, and in the spine, it may cause irreversible neurological conditions [2-6]. Therefore, physicians in all departments involved in patient consultation need to be able to recognize DAVF conditions. Patients with suspected DAVF based on their clinical symptoms should have a head MRI at an early stage or need to be referred to a secondary medical institution. The sub-analysis of Eye symptoms showed a prolonged number of consultation days in MU areas compared to MAS areas. Days (1stDr-1stMR) could be shortened, leading to sDAVF diagnosis at an early stage by engaging in awareness-raising activities of DAVF, such as lecture programs targeting physicians in the medical districts that may not be sufficiently knowledgeable about DAVF, and through the creation of an environment that facilitates referral of patients to NS in base hospitals.

LIMITATION

The limitation of the present study was the small sample size for analysis, since sDAVF is a lowprevalence condition.

CONCLUSION

Since the delay in diagnosing sDAVF may lead to symptoms of irreversible neurological damage, it is crucial to avoid diagnostic delays. MRI is the most important stage that leads to sDAVF diagnosis. Therefore, it is important to raise awareness of DAVF among local community health clinics, including physicians in general practice, to broaden their understanding of DAVF. For eye, ear, and HA symptoms that do not lead to a diagnosis, it is crucial to proactively pursue MRI screening.

DECLARATION OF NO CONFLICT OF INTEREST

All the authors declare that they have no conflict of interest.

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