A multicenter epidemiological study of central nervous system hemangioblastomas in von Hippel-Lindau disease in Japan

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BACKGROUND AND AIM

Cerebellar HBs　Spinal cord HB　Brainstem HB

Central nervous system (CNS) hemangioblastoma (HB) is one of the most common manifestations in von Hippel-Lindau disease (VHL), but large-scale epidemiological studies have scarcely been done. The aim of this study is to clarify the clinical features of CNS HBs in a large number of patients with VHL.

OBECTS AND METHODS

・VHL patients were gathered by the Japanese VHL Study Group in the Japanese Health & Labor Ministry during 2009-2010 via the results of a questionnaire answered by Japanese neurosurgeons at 1020 hospitals.

・The clinical diagnosis for VHL

1) In the presence of a positive family history, a patient with at least one typical VHL tumor, retinal or CNS HB; RCC; PhC; Pancreatic tumor(PT); ELST; and multiple pancreatic cysts.

2) In patients with a negative VHL family history, they exhibit two or more CNS HB or a single HB in association with a visceral tumor such as RCC, PhC, and PT.

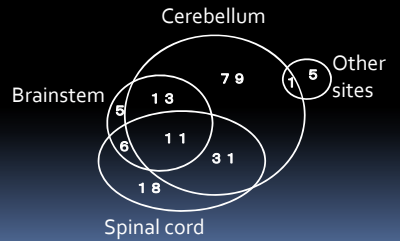
Among the collected VHL patients, those bearing CNS HBs were investigated with respect to the following patients' characteristics

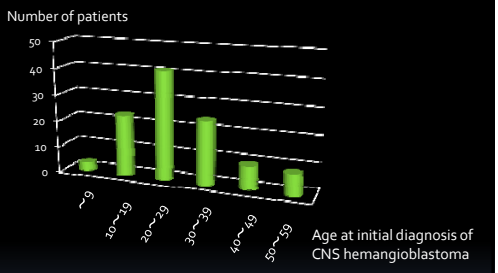
・ Location of CNS HB
・Age of initial diagnosis of CNS HB
・Follow-up period
・Number of operations for CNS HB
・Performance status (PS) assessed according to the (Eastern Cooperative Oncology Group)ECOG.
・ Relationship between the number of operations and the PS or age of the initial diagnosis of CNS HB.

Characteristics of VHL patients bearing CNS HBs

Male/female	81/88
Period of follow-up (mean years±s.d.)	15.2±9.6
Number of VHL patients bearing CNS HBs	169
Patients with cerebellar HB	136 (80.5%)
Patients with brainstem HB	34 (20.1%)
Patients with spinal cord HB	63 (37.3%)
Patients with pituitary HB	3 (1.8%)
Patients with supratentorial HB	3 (1.8%)

Total number of CNS HBs	436
Cerebellum	285(65.4%)
Spinal cord	97(22.2%)
Brainstem	48(11.0%)
Pituitary	3(0.7%)
Suprastentorial	3(0.7%)





The age at initial diagnosis of CNS HB ranged from 7 to 73 years, with the mean being 29.1±12.6 years

Age at initial diagnosis of CNS HB (mean years±s.d.)

Patients with a single HB	34.4±15.8	
Patients with multiple HBs	25.7±9.8	(P<0. 001).

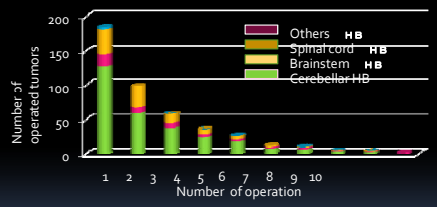
・Similarly, the mean age at the initial diagnosis of patients bearing a single cerebellar HB (33.8 ±15.0 years) was significantly higher than that of patients bearing multiple cerebellar HBs and/or HBs at another site (26.2 ±8.9 years).

・Likewise, in the case of patients bearing a single spinal cord HB, this mean age (35.9 ±17.5 years) was significantly higher than that of patients bearing multiple spinal cord HBs and/or HBs at another site (24.4 ±12.1 years old) (P<0.01).

Operations

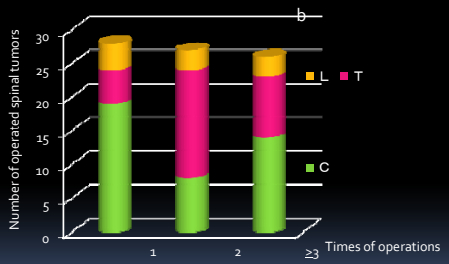
Total number of operations 399

Number of operations per patient (mean ±s.d.) 1 to 10 (2.5±1.9)



Sites of CNS HBs with respect to operation number are shown. Cerebellar HBs were always the most dominant, and the proportion of spinal cord HBs increased with operation number

Spinal cord tumor operations

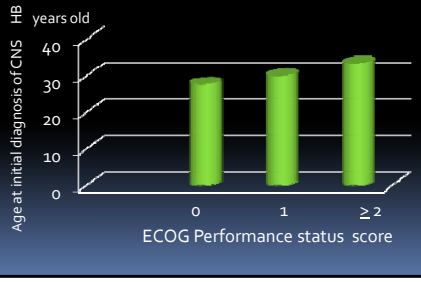


Number of spinal cord HBs with respect to spinal level and operation number. In the first operation, the cervical level was the most dominant location; whereas in the second, the thoracic was the most dominant one.

ECOG Performance status (PS, mean score±s.d.) 0.68±1.04

Relationship between age at initial diagnosis of CNS HB and ECOG performance status. There was a tendency for a positive correlation between the 2 parameters, but no significant correlation (P=0.06).

ECOG PS 0	99 (58.6%)
ECOG PS 1	45(26.6%)
ECOG PS 2	12(7.1%)
ECOG PS 3	9 (5.3%)
ECOG PS 4	4(2.4%)



Relationship between operation number and ECOG performance status score or age at initial diagnosis of CNS HB. The ECOG performance status score was significantly positively correlated with the number of operations, whereas the age at initial diagnosis was inversely correlated with it.

DISCUSSION

・The HB distribution in this present study is similar to that found in previous studies. Spinal cord HB or brainstem HB is frequently also associated with an HB at some other sites, mostly cerebellar HB; whereas cerebellar HB is less frequently associated with HBs at other locations.

・Our findings suggest that spinal cord or brainstem HB is usually an accompanied manifestation of cerebellar HB and that cerebellar HB is often an independent pathology. In other words, when a spinal cord HB or a brainstem HB is found in a patient, such a patient should be predicted to have another manifested lesion associated with VHL, particularly a CNS HB; and this possibility should be explored.

・This present study showed that VHL patients will probably have only a single HB when the age at initial diagnosis of CNS HB is over 30 years, but they will have multiple HBs when initially diagnosed under the age of 30 years. This result indicates that scheduled follow-up is necessary if initial diagnosis is at a young age, but it is not always necessary if initial diagnosis is made over 30 years of age.

・In addition, the present study also showed that the ECOG performance status score was positively correlated with the number of operations and with the age at initial diagnosis of CNS HB.

・VHL patients frequently undergoes multiple operations for CNS HBs, but multiple operations aggravate performance status. If possible, number of operation for CNS HBs had better be reduced.

・When a CNS HB is identified, and the patient is diagnosed as VHL at an age under 30 years, we can thus predict that another HB will appear in the CNS in the future. In contrast, when a CNS HB is identified and the patient is diagnosed as VHL over 35 years of age, we can predict that another CNS HB will not appear later.

Acknowledgement

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