Therapeutic strategies for central nervous system hemangioblastomas in von Hippel-Lindau disease

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CNS hemangioblastoma (HB) in VHL

✔️ 70~80% of VHL patients are associated with CNS HBs.
✔️ CNS HB is the first or second manifestation in VHL patients.
✔️ CNS HSs develop since young age but less frequently do in elderly VHL patients.
✔️ Growth patterns of CNS HBs are mostly saltatory.
✔️ Distribution: Cerebellum 50%, Spinal cord 40%, Brainstem 10%

How to manage CNS HSs with VHL?

✔️ For symptomatic tumors, Surgical resection. Alternatively, stereotaxic radiotherapy (SRT) or pharmacological treatment
✔️ For asymptomatic tumors, Observation and follow-up with annual MRI. If a tumor shows rapid growth, consider surgery.

Subject: 44 VHL patients (29 families)

Male : female = 26 : 18
Age range 9~66 years old
Mean onset age 29.1 years old
Mean follow-up period 9.4 years
Sites of mutations in VHL gene in VHL patients with CNS HBs

Missence mutation is the most common.

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Total number of CNS HBs: 155 (mean 3.6)

Cerebellum 79 (51.0%)
Spinal cord 58 (37.4%)
Brainstem 14 (9.0%)
Pituitary stalk 2 (1.3%)
Cerebrum 2 (1.3%)

Therapies for CNS HBs in VHL patients
Surgical operation alone -------------- 31 patients
Surgical operation & Stereotactic radiotherapy--11
Stereotactic radiotherapy alone------ 2
Pharmacological therapy ----- 0

Times of surgical operations (mean 1.7 times)
1 operation------------------21 patients
2 ---------------------------- 12
3 ---------------------------- 4
4 --------------------------- 3
5 ------------------------ 2
Outcome of surgical operations

Number of VHL patients undergone surgical operations—42

Postoperative ECOG PS score (Eastern Cooperative Oncology Group performance status)

- Grade 0: 34
- Grade 1: 4
- Grade 2: 2
- Grade 3: 1
- Grade 4: 1

✔ Decrease of ECOG PS score correlates with times of operations.
✔ Postoperative ECOG PS correlated with age.

Disappearance of tumor: 2
Shrinkage of tumor: 3
No change after SRT: 5
Peritumoral edema after SRT: 3
(Operations are required for 2 cases among 3)

Outcome of stereotactic radiotherapy (SRT)

Number of VHL patients undergone SRT—11

- Disappearance of tumor: 2
- Shrinkage of tumor: 3
- No change after SRT: 5
- Peritumoral edema after STR: 3
(Operations are required for 2 cases among 3)

Multiple cerebellar HB with VHL, 29y/o M

The 3rd operation at 11 years after the first operation for CNS HB. After the operation, cerebellar ataxia was shown.

Multicystic cerebellar HBs with VHL, 47y/o, F

Past history: Renal cell carcinoma
Family history: Mother VHL

Intraoperative ICG angiography
Multiple cystic CNS HBs with VHL, 15y/o F
Past history: 7y/o, 10y/o operation for cerebellar HBs
Family history: Mother, VHL

After surgery, she showed mild left hemiparesis of upper extremity.

Surgery for cystic cerebellar & brainstem HBs

Surgery for cervical cord HB

Flow chart of therapeutic strategy for CNS HB in VHL
(Japanese therapeutic guideline 2012)

CNS HB
Symptomatic?

- Yes: Cerebellar tumor: more than 2cm or rapid expansion of cyst
- No: Spinal tumor: more than 1cm or enlargement

- Yes: Surgery or SRT
- No: Follow-up with annual MRI
Surgical resection is the first-choice therapy for cerebellar and spinal cord HBs except for intramedullary brainstem HB. The risk of deterioration after the operation is mostly rare.

The operation is principally performed after symptomatic, but the operation should be considered if rapid enlargement of asymptomatic HB is found. The saltatory growth pattern of CNS HB should be understood.

The stereotactic radiotherapy is the second choice therapy for CNS HBs.

Conclusion

Thank you for attention!