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Brief Note

Multicentric Cryptic Cerebellar Hemangioblastomas

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Cerebellar hemangioblastomas[1-7] are relatively uncommon ; their incidence is about two per cent of all brain tumors. They occur mainly in young adults, and ten to twenty per cent of these are familial. They are occasionally accompanied by angiomatoses of the retina (von Hippel's disease), and congenital cysts or tumors of the general organs such as the pancreas, kidneys and liver. This condition is known as von Hippel-Lindau disease. Sometimes they show erythrocytosis.

These neoplasms may be multiple[8-10]. Recently, by postmortem examination, we found many cryptic hemangioblastomas in the remaining cerebellum of a patient who had undergone surgical extirpation of two manifest hemangioblastomas on separate occasions. This case was thought to be a suitable example for considering the histogenesis of the cerebellar hemangioblastoma.

The patient was a 23-year-old female (Chart No. A-8472 ; Autopsy No. A-20). Five other members of the paternal side of her family extending over three generations had been affected with cerebellar hemangioblastomas. Her first cerebellar hemangioblastoma was totally removed 9 years and 8 months before her death[11]. The tumor was situated in the subcortical region of the lateral inferior part of the right cerebellar hemisphere. It was 2 g in weight and $1 \times 2 \times 1$ cm in size, with a large cyst containing 50 ml of fluid. The second discrete tumor spreading over the inferior portion of the vermis and left cerebellar hemisphere was removed 9 years and 8 months later, and 7 days before her death. It was solid, its weight was 5.2 g and the size was $2.9 \times 2.3 \times 1.4$ cm. Both tumors were histologically typical capillary hemangioblastomas. They were composed of networks of blood vessels of variable sizes showing mature capillaries or cavernous structures lined by a single layer of endothelial cells. Among these mature vascular channels there were many large stromal cells with foamy cytoplasm and prominent nucleus (Fig. 1).

Although macroscopic mass lesions were not apparent at autopsy, microscopic examination with serial vertical sections of a 2.4 mm thick horizontal section of the entire right and left cerebellar hemispheres and vermis demonstrated seventeen independent cryptic hemangioblastomas in all. Six of these were located in the right cerebellar hemisphere, seven in the left cerebellar hemisphere and four in the vermis. This does not include a small amount of neoplastic tissue left at the second operation. It is probable that many more cryptic tumors could be found with more extensive examination.

The largest nodule was 1,560 microns, while the smallest one was 240

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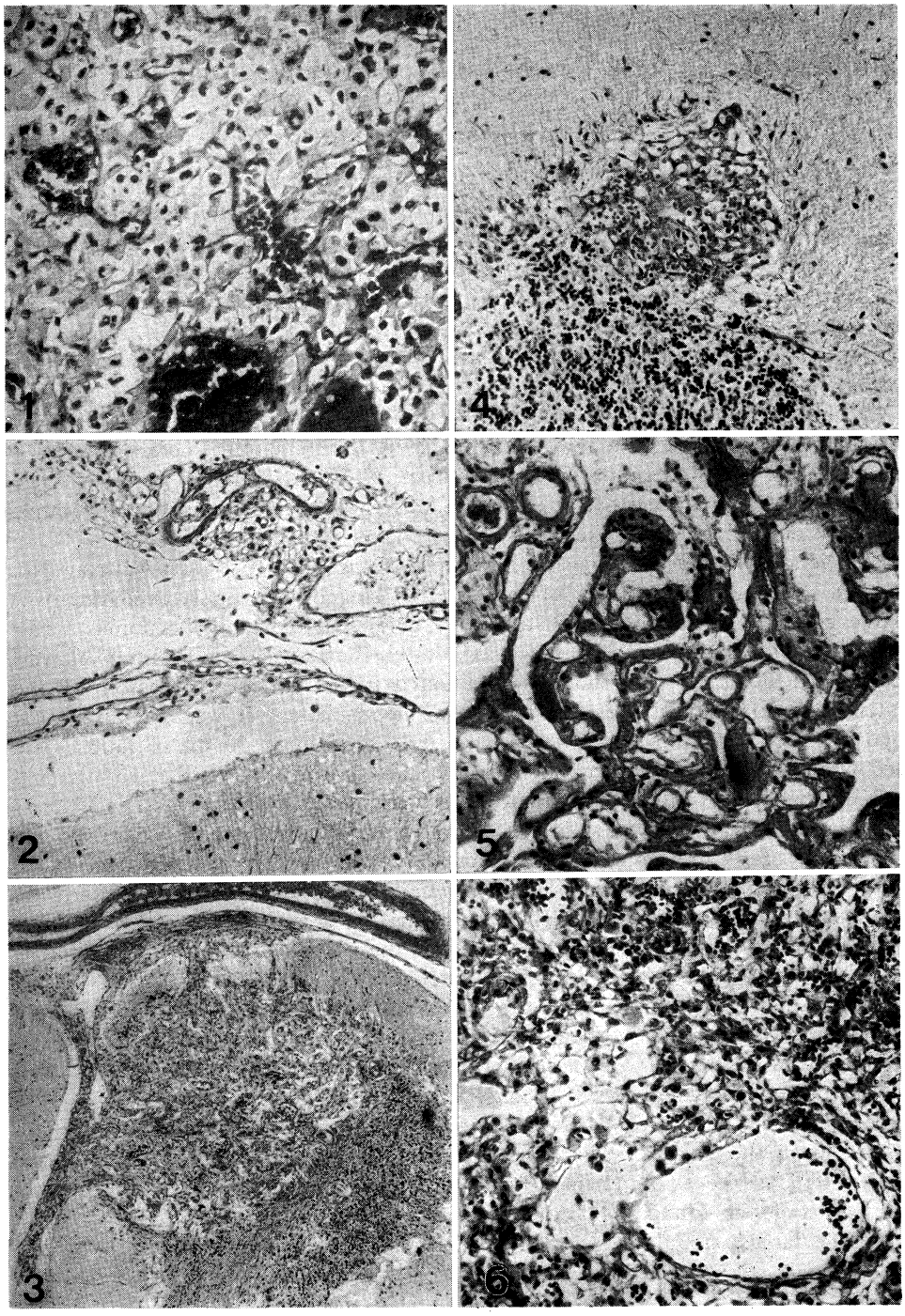
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Fig. 1. Photomicrograph of the tumor removed during the second operation. Numerous mature capillaries and cavernous structures are seen. Between them there are stromal cells with foamy cytoplasm and prominent nucleus. ×158, H&E.
Fig. 2. Tumor localized in the pia-arachnoid. It is composed almost completely of mature capillaries and also a few mature meningeal veins. ×122, H&E.
Fig. 3. Photomicrograph of the tumor extending over the cerebellar cortex and pia-arachnoid. ×48, H&E.
Fig. 4. Small nodule, which is composed exclusively of mature capillaries, restricted to within the Purkinje cell layer. ×122, H&E.
Fig. 5. Tumor found in the choroid plexus. There is a nest of capillaries between mature blood vessels and connective tisssue of the choroid plexus. ×158, H&E.
Fig. 6. Photomicrograph of the tumor within the cerebellar cortex showing capillaries and cavernous structures with some stromal cells. ×158, H&E.

microns in its largest dimension. The tumors were found in various locations ; some were entirely localized in the pia-arachnoid (Fig. 2), some extended over the cerebellar cortex and pia-arachnoid (Fig. 3), some were restricted to within the cerebellar cortex (Fig. 4), and some were spread over the cerebellar cortex and its adjacent subcortical white matter. There were no tumors in the deep white matter of the hemispheres around the dentate nuclei. One was found in the choroid plexus attached to the inferior medullary velum (Fig. 5).

Histologically these cryptic hemangioblastomas contained less cavernous structures and foamy stromal cells than the manifest tumors removed operatively before the patient's death (Fig. 6). Especially small ones less than 500 microns were composed almost exclusively of mature capillaries. There were no capsules, and fibrillary astrocytes had invaded between these capillaries. Cerebellar parenchyma surrounding these tumor tissues occasionally had become loose and formed many microcysts. Syringobulbomyelia was observed in the medulla and upper cervical cord. Other pathological findings have been reported elsewhere[12].

According to Lindau[13] and other investigators[14,15], the histogenesis of cerebellar hemangioblastomas has been considered as follows. The capillaries are made phylogenetically from the vascular mesenchymal plate during the third fetal month. At about the same time the cerebellar hemispheres are formed and developed laterally, and primitive vascular mesenchymal tissues extend toward the cerebellar hemispheres. Abnormal capillaries are embedded in the cerebellum because of capillary maldevelopment at this period, and they may be the origin of cerebellar hemangioblastomas. In these anomalous capillary nests, stromal cells, which are said to be vasoformative cells derived from the capillary endothelial cells, may proliferate and become neoplastic.

At around the same time, capillaries are formed in the retina, and the pancreas is also formed. Accompanying developmental abnormalities of these organs have been explained as well by fetal abnormalities of this period. In addition, the cerebellar hemangioblastoma may be accompanied by syringobulbomyelia as another congenital anomaly.

As to the original site of these cerebellar hemangioblastomas, the intimate relationship with the pia-arachnoid has been stressed[7]. According to our

observations in this autopsy case, manifest hemangioblastomas may arise in any part of the cerebellum, such as in the pia-arachnoid itself, pia-arachnoid and the cerebellar parenchyma, or within the cerebellar parenchyma of the hemispheres or vermis. They may be situated even in the choroid plexus. The occurrence in the deep white matter of the cerebellar hemispheres around the dentate nuclei, however, may be relatively rare.

Thus, as these tumors may be multicentric as in the present case, strict follow-up may be necessary even after total removal of the tumor, especially in familial instances.

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REFERENCES

1) Cramer, F. and Kimsey, W. : The cerebellar hemangioblastomas. Review of fifty-three cases, with special reference to cerebellar cysts and the association of polycythemia. Arch. Neurol. Psychiatry **67** : 237-252, 1952
2) Olivecrona, H. : The cerebellar angioreticulomas. J. Neurosurg. **9** : 317-330, 1952
3) Mondkar, V.P., Mckissock, W. and Russell, R.W.R. : Cerebellar hemangioblastoma. Br. J. Surg. **54** : 45-49, 1967
4) Sano, K., Kuwabara, T., Sato, O., Nagai, M., Takizawa, T. and Kyaw, A. : Hemangioblastomas of the brain. Brain Nerve (Tokyo) **19** : 643-653, 1967 (in Japanese)
5) Kinoshita, K., Matsukado, Y. and Nakayama, T. : Cerebellar hemangioblastoma. So-called Lindau's disease or Lindau's tumor. Jpn. J. Clin. Exp. Med. **48** : 2588-2594, 1971 (in Japanese)
6) Palmer, J. J. : Haemangioblastomas. A review of 81 cases. Acta Neurochir. **27** : 125-148, 1972
7) Russell, D.S. and Rubinstein, L.J. : Pathology of tumours of the nervous system, 4th ed. London, Edward Arnold. 1977, pp. 116-127
8) Pennybacker, J. : Recurrence in cerebellar haemangiomas. Zentralbl. Neurochir. **14** : 63-73, 1954
9) Stein, A.A., Schilp, A.O. and Whitefeld, R.D. : The histogenesis of hemangioblastoma of the brain. A review of twenty-one cases. J. Neurosurg. **17** : 751-761, 1960
10) Kitano, I., Kinoshita, K., Fukumura, A. and Matsukado, Y. : Familial multiple hemangioblastomas. Report of two cases in a family. Neurol. Surg. **5** : 611-617, 1977 (in Japanese)
11) Umeda, A., Ueda, S. and Kajitani, T. : A case of cystic hemangioblastoma of the cerebellum with heavy heredity in the family tree. Brain Nerve (Tokyo) **18** : 923-928, 1966 (in Japanese)
12) Koga, A., Seki, Y., Tsutsui, J., Shirabe, T., Fukai, H., Nakajo, S. and Goto, H. : An autopsy case of postoperative skew deviation. Jpn. Rev. Clin. Ophthalmol. **69** : 1338-1342, 1975 (in Japanese)
13) Lindau, A. : Discussion on vascular tumours of the brain and spinal cord. Proc. R. Soc. Med. **24** : 363-370, 1931
14) Cushing, H. and Bailey, P. : Hemangiomas of cerebellum and retina (Lindau's disease). With the report of a case. Arch. Ophthalmol. **57** : 447-463, 1928
15) Spence, A. M. and Rubinstein, L. J. : Cerebellar capillary hemangioblastoma. Its histogenesis studied by organ culture and electron microscopy. Cancer **35** : 326-341, 1975