CEREBELLAR HEMANGIOMA (HEMANGIOBLASTOMA)
A CLINICOPATHOLOGICAL REVIEW OF 40 CASES*
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In the classical monograph Tumors Arising from the Blood-Vessels of the
Brain, Cushing and Bailey reported 11 cases of “hemangioblastoma”
of the cerebellum. Recent analysis of this cerebellar neoplasm was
made by Cramer and Kimsey who presented the clinical findings in a larger series
of cases, in 37 of which the tumor was histologically verified. The present
paper describes the clinical and pathological findings in 40 cases of this neo-
plasm, which we prefer to designate “hemangioma” of the cerebellum. We
use this term, as others have in the past, in place of the name “hemangio-
blastoma” proposed by Cushing and Bailey, for reasons that will be pre-
sented below.

CLINICAL ASPECTS

There is no predilection for either sex. In our series, there are 24 males and
16 females. The age incidence was from 3 to 62 years of age, the highest
falling in two decades, the third and sixth (Fig. 1). The average age was 36.2 years. Only one mem-
ber of the group belonged to the colored race.

The commonest presenting symptom was headache. Other manifestations of an expanding le-
son of the posterior fossa were noted, such as ataxia, vertigo, vomiting and blurring of vision.
Choked disc was present in 85 per cent of the cases. The average duration of symptoms prior to
operation was 10 months.

All of the group were patients at the Johns Hopkins Hospital. Thirty-one were operated upon by Dr. Walter E. Dandy, the remainder by
other attending or resident surgeons of the hospital staff. In view of the vari-

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atation in surgical technique, a detailed analysis of mortality is not warranted.

The operative mortality for the group was 20 per cent, 2 patients dying shortly after admission before operation could be performed. Of the 30 patients surviving surgery, 7 are now dead, having had an average survival period of 10.7 years; the life expectancy in this group, as computed from actuarial tables, is 37 years. At least 2 of the patients died from causes unrelated to the tumor. Twenty-three patients are still alive and their average survival to date is 6.2 years. The 5-year survival rate, commonly applied in the analysis of tumor surgery, is 50 per cent.

Nine of the 40 patients were subjected to more than one operation, 2 patients having had four operations. It is not clear whether these reoperations were performed because of independent isolated foci manifesting themselves at a later date, or because of continued growth of incompletely removed tumor tissue.

The late appearance of hemangiomas of the central nervous system in Lindau’s complex is well known. In our series, 9 patients had proven Lindau’s disease, 4 of them requiring multiple operations. This figure of slightly more than 20 per cent in our series of cerebellar hemangiomas agrees with that of Lindau, who found that 20 per cent of the patients with retinal hemangioma (so-called von Hippel’s disease) subsequently were shown to have a cerebellar neoplasm or other evidence of Lindau’s complex. It raises the serious possibility that all patients with a cerebellar hemangioma are suffering from Lindau’s disease in which other members of the pathological complex have not yet appeared.

In the diagnosis of the cerebellar hemangioma, clinical laboratory examinations are of limited value. The cerebrospinal fluid protein seldom is elevated and then only minimally. This is in contrast to the spinal hemangiomas, with which it is exceedingly high. The explanation for this probably lies in the fact that the former are seldom in contact with the subarachnoid space, whereas the spinal lesions almost invariably involve this space.

In examination of the peripheral blood, we found that 40 per cent of these patients had hemoglobin values greater than 15 gm., and in 3 cases values as high as 18.5 gm., with a red blood cell count of 6.3 million, were noted. In none of the cases were blood and plasma volume determinations, arterial oxygen saturations, or bone marrow studies performed, yet in these 3 cases, the clinical diagnosis of polycythemia rubra vera was made and treated by venesection.

**PATHOLOGICAL ASPECTS**

Hemangioma of the cerebellum may be cystic or solid, single or multiple, and situated either in the midline or in the hemispheres. Forty per cent of the tumors showed attachment to the meninges, half of these (8 cases) to the dura, usually to the ventral aspect of the tentorium. Thirty tumors consisted of a nodule with a single large cyst, 4 had a grossly multiloculated cystic appearance, and 6 were solid.
Fig. 2. (A) Relationship of a juvenile-type hemangioma to granular layer of cerebellar cortex. H&E, X100. (B) Growth of tumor in subarachnoid space and white matter of cerebellum. Zone of cleavage between cerebellum and hemangioma is demonstrated. H&E, X30.

Grossly, the majority of the tumors were circumscribed and demarcated from the adjacent cerebellar tissue by a loosely arranged network of glial fibers. This line of demarcation facilitates the removal of the tumors, the superficially placed ones being readily “shelled out” (Fig. 2).

There is considerable variation in the diameter of the cyst. The latter is usually filled with a yellow to brown, gelatinous transudate. Protein values when measured were as high as 5.5 gm. per cent. The mural nodule may be situated in any location in the cyst wall and varied from 0.5 to 5 cm. in diameter. When small, it may be difficult to locate at surgery. Large, promi-
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Cerebellar hemangioma (hemangioblastoma) may be seen coursing over the surface of the cyst. Seldom is the pia mater or dura mater thickened or firmly adherent to the cyst, so that meningeal attachments of the tumor are readily divided.

We propose the following histological classification: (1) juvenile type; (2) transitional type; and (3) clear-cell type.

(1) The juvenile type is predominant in the first three decades of life and is characterized by the presence of thin-walled capillaries lined by endothelium. There is a varying number of dilated vessels and tightly packed capillaries (Fig. 3). Around these capillary-cavernous and blood-filled spaces, one sees a protein coagulum which is most likely transuded plasma (Fig. 4A). This plasma is precipitated by the fixative and in some cases may be abundant, forming a halo of pink-staining finely granular material about the vessels in the hematoxylin and eosin stained sections.

Between the blood vessels are sheets and strands of endothelial cells, identical with those lining the vascular spaces. These cells almost invariably show no variation in size, shape, and staining qualities. Prominent nucleoli and mitotic figures are almost never seen. Mononucleated or multinucleated giant cells are rarely evident (Fig. 4C).

We have chosen the name "juvenile" for this capillary-cavernous he-
Fig. 4. Juvenile-type hemangioma. (A) Protein coagulum in intercapillary space (microcyst). H&E, ×600. (B) Capillaries, outlined by reticulin. Reduced silver, ×600. (C) High power view of cell types. H&E, ×600.
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mangioma, not only because it occurs in the younger age groups, but because microscopically it represents the earliest picture designated by the term “hemangioma,” that is, a benign tumor forming blood vessels. As will be described below, this uniform and monotonous picture changes with time, and the development of hemorrhages, transudates, cyst formation, and periods of rapid growth. Some authors have suggested that with the passage of time, the neoplasm undergoes a sclerosing and obliteratorive process. In our material, we have failed to demonstrate by special stains the development of abundant connective tissue between the vessels, comparable to the scleros-

Fig. 5. Transitional-type hemangioma. (A) Endothelial cells with pale-staining cytoplasm. Occasional large nuclei or multinucleated cells are present. H&E, ×200. (B) There is wide variation in size and shape of endothelial cells, and suggestion of alveolar arrangement of clear cells. H&E, ×100.

ing type of hemangioma of the skin. Instead, silver stains reveal abundant reticulin adjacent to the capillary walls (Fig. 4B).

(2) Transitional type. With the development of hemorrhages within the tumor, there is a response on the part of the endothelial cells. They undergo hyperplasia and utilize their phagocytic power to engulf the red cells and coagulated serum. They swell up and become filled with sudanophilic (lipid) material. This takes the form of large globules and finely dispersed lipids. These xanthoma cells then have a clear or pale-staining cytoplasm, with a centrally placed nucleus. The presence of lipids in the cell cytoplasm was confirmed by utilizing tissue fixed in 10 per cent formalin, cutting frozen sec-
Fig. 6. Clear-cell type hemangioma. (A) Pseudotubular (alveolar) arrangement. The entire tumor showed this uniform appearance. H&E, ×100. (B) Another example, with the cells separated by a reticulin framework. H&E, ×100. (C) Frozen section of tumor in (B) stained for fat. Dark granules are sudanophilic. Sudan IV, ×100.
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tions, and staining them with Sudan IV. In this category, the term “transitional” was chosen to signify a transition from the juvenile to clear-cell type. The absence of cytoplasmic staining appears to be the result of the extraction of engulfed lipids in the routine preparation of hematoxylin and eosin sections. In this type, a few to moderate numbers of large mononucleated giant cells appear, microcysts become prominent, and there are areas of hemorrhage. Thus, the uniform appearance of the juvenile type is lost (Fig. 5).

Fig. 7. Correlation of age of patient and cell-type of tumor in 40 cases of cerebellar hemangioma. The predominance of the juvenile type in the younger age groups, and the transitional and clear-cell types in the older age groups is noted.

(3) Clear-cell type. The last category comprises the group in which the neoplasm is made up almost entirely of xanthoma cells (Fig. 6). In our series, these tumors occurred with but one exception in the older age groups. In several of the patients who had “recurrences,” a change from juvenile type, through transitional cell, to clear-cell type was noted.

Histologically, the usual pattern is one of sheets of cells with a rich vascular stroma. In some of the tumors, however, there are pseudotubular formations around a blood vessel. Giant cells and abundant microscopic cysts become prominent.

The microscopical picture is to be differentiated from that of a metastatic hypernephroma. In this regard, mitotic figures and prominent nuclei may prove of value in the diagnosis, as they do not occur with significant frequency in hemangioma but are common in the more undifferentiated types of hypernephroma. However, it appears very difficult, if not impossible, to distinguish clear-cell hemangioma of the cerebellum from the well-differentiated types of metastatic clear-cell hypernephroma.
The correlation of the various histological types with the ages of the patients is shown in Fig. 7. It may be noted that the second peak of incidence corresponds to a predominance of transitional and clear-cell forms of the tumor occurring in the older age groups.

DISCUSSION

The diagnosis of hemangioma of the cerebellum should be considered in every patient presenting signs or symptoms of an expanding lesion of the posterior fossa.

As emphasized by Lindau,\(^5\) and Cushing and Bailey,\(^4\) the presence of a cerebellar neoplasm in a patient with (a) familial history of angiomatous disorder or (b) evidence of involvement of another organ, as seen in Lindau’s complex, permits the pre-operative diagnosis of this neoplasm. The patient’s age may indicate a reasonable estimate of the degree of differentiation of the tumor.

The fact that this cerebellar neoplasm, when occurring as an isolated tumor, is indistinguishable from the cerebellar hemangioma of Lindau’s disease, raises the possibility that a similar etiologic factor, heredofamilial in nature, underlies this condition.

There has been considerable speculation in the literature (most recently by Tonning, Warren, and Barrie\(^6\)) regarding the etiology of the neoplastic transformation in this vascular tissue. They regard it as a “fundamental persistent lack of integration between blood vessels and parenchyma.” We concur in viewing the disease as a dynamic process superimposed upon a heredofamilial developmental defect. The chronological transition of the tumor from juvenile to clear-cell type describes a life-history for this neoplasm which lends itself to logical classification. This classification is offered in place of the previously used “solid” or “cystic” categories, the latter referring to a presumed coalescence of smaller cavities into a larger cyst.

Our conception of the growth-potential of these neoplasms ascribes to them a limited capacity for proliferation. We note the infrequency of mitotic figures, the loose cellular structure, the increasing deposition of hemosiderin and lipids, and the late appearance of mono- or multinucleated giant cells, all as evidence of low or absent cytological malignancy. For these reasons, we feel that the term “hemangioblastoma” conveys a false conception of malignant potentiality and primitive structure for a tumor that we believe to be more appropriately classified as “hemangioma,” a benign tumor of adult tissue.

In all of our cases, save one, there has been no evidence whatsoever suggestive of hematopoiesis within the tumor. An intensive search for erythropoiesis in all sections from the entire series was unsuccessful in demonstrating such foci, except in a single case in which polycythemia rubra vera had not been ruled out.

The relationship between cerebellar hemangioma and so-called polycythemia has been noted by a number of authors.\(^2,3\) There is no satisfactory
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explanation for the occurrence of an elevated red cell count in the peripheral blood in association with cerebellar hemangioma. It is interesting, however, that a high incidence of erythrocytosis has not been noted with any other intracranial lesion. Review of a large series of astrocytomas by the authors failed to disclose any erythrogenic tendency. Further hematologic studies are required to evaluate this erythrogenic tendency in association with other vascular tumors of the brain. (The term erythrocytosis seems preferable to polycythemia, as the latter implies neoplasia of the erythropoietic tissue, for which the term polycythemia rubra vera is reserved.)

The clinical manifestations of cerebellar hemangioma are but little dependent upon the specific nature of the growth, and largely dependent upon the location and size of the lesion, especially with respect to obstruction of the ventricular system. Treatment, therefore, is entirely a neurosurgical problem, with subsequent irradiation having no clear-cut effect upon the course of the illness.

In our histological studies, we have not been impressed with multicentricity of the lesions as stated by Cramer and Kimsey. It would seem likely that "recurrence" of the tumor is the result of incomplete removal, whether caused by mechanical failure of complete removal at the operative site, or failure to recognize adjacent tumor tissue. The latter is always a possibility due to the wide variation in gross appearance of hemangiomatic tissue. Complete removal, which is frequently difficult, should not be followed by "recurrent" tumor.

The development and significance of the clear-cell type of cerebellar hemangioma is worthy of emphasis because this type may be confused microscopically with metastatic hypernephroma of the kidney by the pathologist unaware of its characteristics.

SUMMARY

The cerebellar hemangiomas are benign, usually cystic, but occasionally solid neoplasms which may become manifest at any age. Surgical removal offers an excellent prognosis.

The relationship to Lindau's disease, as well as to erythrocytosis, should always be investigated in the hope of throwing further light upon the interrelationships among these conditions.

The varied histological appearance of the cerebellar hemangioma should be recalled so as to avoid a mistaken diagnosis of a malignant or metastatic lesion.

The analysis of 40 histologically verified hemangiomas of the cerebellum permits classification of these lesions as juvenile, transitional or clear-cell in type, based upon the stage of development of the tumor.

This paper is dedicated to Professor Percival Bailey, on the occasion of his 60th birthday.

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REFERENCES


