MEDULLOBLASTOMA CEREBELLI

A COMMON TYPE OF MIDCEREBELLAR GLIOMA OF CHILDHOOD *

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In previous communications from this clinic, it has been pointed out that the true tumors of the central nervous system represent about 40 per cent. of all intracranial neoplasms. Considered as a group, these lesions usually receive the pathologic diagnosis of glioma; this unqualified term implies to many a condition of hopeless malignancy. However, the fact has gradually become appreciated that certain types of glioma are favorable to operative removal and others are favorably influenced by radiation. It consequently is important, more especially for the neurosurgeon, on both prognostic as well as therapeutic grounds, that his clinical experiences should be correlated with a more detailed classification of the gliomas than is customary.

This is a task the authors have set for themselves,[1] and in the course of a preliminary survey of the material at hand, representing the records and tissues of approximately 400 gliomas, we were impressed by the frequency with which there has been encountered (in the large majority of cases in childhood) a very cellular tumor of a peculiar kind, apparently arising over the roof of the fourth ventricle and projecting into the center of the cerebellum.[2]

Accordingly, under the designation of spongioblastoma cerebelli, a series of twenty-five of these tumors was reported at the 1924 meeting of the American Neurological Association. In this terminology we had followed Ribbert,[3] unaware at the time of preparing our paper that

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* From the Surgical Clinic of the Peter Bent Brigham Hospital.

* Presented at the Fiftieth Annual Meeting of the American Neurological Association, Philadelphia, June 5, 1924.

1. The expenses of these researches have been defrayed by the Philip Gray Fund for the Study of Brain Tumors.

2. Five other tumors unquestionably of the same histogenesis have been encountered among the many gliomas of the cerebral hemispheres. One of these had spread widely through the leptomeningeal spaces forming the picture of the so-called "sarcomatosis of the meninges." The tumors therefore cannot be said to be confined to the region of the fourth ventricle though the percentages show this is by far the more common site, more particularly in children. All four cerebral cases were in adults.

3. Ribbert: Ueber das Spongioblastom und das Gliom, Virchows Arch. f. path. Anat. **225**:195, 1918.

Strauss and Globus had previously and independently of Ribbert employed the identical term.[4]

At the same meeting, Globus and Strauss gave a report on a series of spongioblastomas of the cerebrum, in which the growth shows considerable cellular differentiation not present in the group of cerebellar tumors we had under consideration. It was evident both to these gentlemen and ourselves that it would be unfortunate to confuse the issue by publishing the papers as they stood without modification of the titles; consequently, after interviews with them and a study of their specimens, we shall adopt for our cases the term *Medulloblastoma* as appropriate to the particular tumors to which we independently desire to call attention.

The undifferentiated medulloblastomas to which we shall confine our present discussion have long been recognized as having an unmistakable microscopic appearance which sets them apart from all other tumors of the glioma series. In our Brigham Hospital records, as will be seen, many of them have in the past been designated neurocytomas or neuroblastomas,[5] under what we now believe to be a mistaken conception of their histogenesis. This was partly due to the fact that by the methods of staining for glia in common use the inconspicuous cell processes found in these tumors did not stain like neuroglia, and consequently they were regarded on this negative evidence as probably of neuroblastic origin. However, by the adoption of the more precise methods for staining the processes and fibrils of glia cells introduced by the Spanish school, it has been possible to demonstrate that the cells of these tumors, though in large part undifferentiated, are potential gliocytes rather than neurocytes. This finding serves not only to exclude them from the extremely rare tumors composed in large part of what unquestionably are neuroblasts, but also to exclude them from the group of sarcomas, an equally rare tumor of the nervous system with which they have by many been confused.[6]

4. Strauss, I., and Globus, J. H.: Spongioblastoma with Unusually Rapid Growth Following Decompression, Neurol. Bull. **1**:273, 1918.

5. These terms were introduced fifteen years ago by J. Homer Wright (J. Exper. Med. **12**:556-561, 1910). All of the twelve tumors which he then reported had presumably originated from the anlage of the abdominal sympathetic system (suprarenal) with the single exception of his Case XI, which proves to be No. 3 of our present series of cerebellar medulloblastomas. The tendency of the cells in the suprarenal tumors toward a roset arrangement, a tendency which is also present in the tumors of the central nervous system under discussion, has been the histologic feature of the lesion on which the diagnosis of neuroblastoma has in large part subsequently been based.

6. Ford, Frank R., and Firor, Warfield M.: Primary "Sarcomatosis" of the Leptomeninges, Bull. Johns Hopkins Hosp. **35**:65-75 (March) 1924.

The tumors, to be sure, are made up of rapidly growing undifferentiated cells resembling those of a round cell sarcoma. But if it can be shown that they are of ectodermal origin and correspond to the undifferentiated cells in the developing cerebellum, their histogenesis is thereby established, and the terminology proposed may well be adopted as appropriate for them.

STAINING METHODS

In order, therefore, to determine whether the cells composing these tumors were of mesodermal or ectodermal origin, and if ectodermal, as was presumed, whether they belonged to the spongioblastic or neuroblastic series, the following methods were employed for displaying the structural characteristics (1) of nervous tissue, (2) of connective tissue, (3) of neuroglia.

If the material had been fixed in Zenker's fluid, it was embedded in paraffin, and the sections were stained with hematoxylin and eosin, Mallory's phosphotungstic acid-hematoxylin, Mallory's anilin blue-orange G, neutral ethyl violet-orange G, and Held's methylene blue-erythrosin. In this way it was possible to identify collagen, reticulum, fibroglial fibrils, neuroglial fibrillae and tigroid substance. There is no way known to us whereby neurofibrillae can be identified in material fixed in Zenker's fluid.

Most of the tissues had been preserved in 10 per cent. formalin, and on this the following methods were employed on frozen sections cut from the same block:

(*a*) For collagen and reticulum, Perdau's method.

(*b*) For neuroglial fibrillae, Hortega's first variant.

(*c*) For protoplasmic glia, Achúcarro's tannic silver method and Hortega's fourth variant.

(*d*) For neurofibrillae, Bielschowsky's method and a recent method of Cajal.

(*e*) For tigroid substance, the method of Bielschowsky-Plein.

For the identification of neurofibrillae, Bielschowsky's method was always used after treatment with pyridin, and even then the sections were always carefully compared with preparations made by the method of Perdrau, for the reticulum of the connective tissue is often sharply impregnated by the method of Bielschowsky. The Bielschowsky preparations were also carefully compared with the Cajal sections.

For the identification of the neuroglia we depended always on Achúcarro's tannic-silver method, which never impregnates nerve fibers. There is no need to compare these with Perdrau preparations, since the intensely black reticulum is easily distinguished from the more delicate neuroglial fibrillae. These fibrillae, as a rule, especially the embryonic ones, are golden brown, though when fully differentiated they may

also appear black. Since these preparations are difficult to photograph, others were made with Hortega's fourth variant at the same time. These have the advantage of lending themselves better to reproduction, but they cannot be relied on to identify neuroglia since axons are impregnated as well.

Achúcarro's method was used in the following way:

(1) Cut frozen sections of formalin-fixed tissue at 10 microns.

(2) Heat to steaming in a 10: 100 solution of pure tannic acid.

(3) Allow to cool. Wash sections in distilled water plus 2 drops of ammonia until they recover their flexibility.

(4) Place in dilute Bielschowsky's ammonia-silver solution (3 or 4 drops to 10 c.c. of distilled water) until the white matter begins to be stained.

(5) Reduce in 20% formalin plus 6-8 drops of ammonia to each 10 c. c.

(6) Wash; dehydrate; clear; mount in balsam.

CASE REPORTS

We are dealing, then, with a well recognized tumor frequently called a neuroblastoma (or when spread through the meninges, a sarcoma), for which we wish to propose a new and more specific term. The tumor is one which may be diagnosed at the bedside with a possible 50 per cent. of accuracy; one which should be capable of type recognition when subsequently exposed at operation; and one for which, when so identified, a generous decompression with subsequent radiation, rather than attempted surgical removal, is the form of treatment to be advocated.

In our original paper prepared a year ago, we had purposely included case reports of the entire series, in order that repetition might serve to emphasize how similar to one another the stories were in all respects—in their clinical history, operative outcome and pathologic findings. This, however, now seems unnecessary, and we consequently have prepared the accompanying table which may give sufficient information for this delayed paper. From the list, which now numbers twenty-nine cases, we have selected for presentation in abstract six examples which will serve to illustrate most of the points we desire to bring out.

The first two cases we present are those in which a fatality occurred without operative intervention. The tissues show the size which the tumor may attain under these circumstances. The pressure effects, both general and local, of a tumor in this situation can be easily surmised. From the first outspoken symptoms, the disease, as will be seen, tends to pursue a rapid course—a matter of a few months.

Cerebellar syndrome with hydrocephalus. Death without operation. Necropsy. Midcerebellar medulloblastoma.

Series of Cases in Which Operation Was Performed

Case	Surg. No.	Sex	Age, Years	Preoperative Symptoms	Operation	Postoperative Survival	Original Diagnosis	Remarks
1	J. H. H. 15498	F	2	9 mo.	Dec. 17, 1903, radical extirpation	4 mo.	Sarcoma	
2	J. H. H. 16736	M	7	5 mo.	Sept. 26, 1904, suboccipital decompression	4 mo.	Gliosarcoma	
3	J. H. H. 24398	F	9	6 mo.	June 13, 1909, partial extirpation	Fatality	Neuroblastoma	
4	J. H. H. 24714	M	6	5 mo.	1. Oct. 5, 1909, suboccipital decompression 2. Oct. 13, 1909, attempted extirpation	Fatality	Neuroblastoma	
5	J. H. H. 25600	M	7	3 mo.	1. March 21, 1910, suboccipital decompression 2. July 19, 1910, attempted extirpation	4 mo. Fatality	Sarcoma	
6	P. B. B. H. 29	M	28	3 mo.	1. March 3, 1913, suboccipital decompression 2. Sept. 15, 1913, partial extirpation 3. June 3, 1914, radical extirpation	21 mo.	Glioma	
7	P. B. B. H. 320	F	6	5 mo.	None; sudden death	.....	Neuroblastoma	
8	P. B. B. H. 1976	F	5	3 yr.?	Oct. 29, 1914, partial removal	3 mo.	Glioma	
9	P. B. B. H. 2175	M	8	4 mo.	Dec. 14, 1914, partial extirpation	2 mo.	Glioma	
10	P. B. B. H. 2527	M	15	2 mo.	None; sudden death	.....	Glioma	
11	P. B. B. H. 2864	M	15	3 mo.	1. May 8, 1915, suboccipital decompression 2. Jan. 21, 1916, radical extirpation	9 mo.	Glioma	
12	P. B. B. H. 3442	M	6	2 mo.	1. Aug. 26, 1915, partial extirpation 2. May 31, 1916, extirpation	10 mo. Fatality	Glioma	
13	P. B. B. H. 5611	M	10	2 mo.	Nov. 3, 1916, suboccipital decompression	16 mo.	Glioma	
14	P. B. B. H. 11606	M	6	9 mo.	Dec. 8, 1919, suboccipital decompression	21 mo.	Neuroblastoma	Series of radium treatments
15	P. B. B. H. 11785	F	27	15 mo.	Jan. 10, 1920, partial extirpation	23 mo.	Neuroblastoma	Two roentgen-ray treatments, with great improvement; spinal metastasis
16	P. B. B. H. 12416	F	3	10 mo.	May 21, 1920, partial extirpation	4 mo.	Glioma	Four roentgen-ray treatments unavailing improvement
17	P. B. B. H. 13981	M	6	7 mo.	Feb. 14, 1921, partial extirpation; removal of arch of atlas	Living	Neurocytoma	Five roentgen-ray treatments; relief for 48 months
18	P. B. B. H. 15555	M	28	2 mo.	Nov. 21, 1921, partial extirpation	Fatality	Neuroblastoma	
19	P. B. B. H. 16059	F	10	2½ mo.	1. Feb. 13, 1922, cyst evacuated 2. May 27, 1922, tumor extirpated	22 mo.	Glioma	Data concerning treatments unavailable
20	P. B. B. H. 17428	M	5	1½ mo.	1. Sept. 30, 1922, suboccipital decompression 2. March 25, 1924, laminectomy	21 mo.	Glioma	Active roentgen-ray treatment; developed spinal metastasis; no return of cerebellar symptoms
21	P. B. B. H. 18793	F	2	3 mo.	May 16, 1923, partial enucleation	12 mo.	Glioma	Three roentgen-ray treatments
22	P. B. B. H. 18901	F	12	12 mo.	1. June 18, 1923, suboccipital decompression 2. June 27, 1924, radical extirpation	12 mo. Fatality	Neurocytoma	Six roentgen-ray treatments
23	P. B. B. H. 19386	M	21	2 mo.	Aug. 22, 1923, partial extirpation	9 mo.	Glioma	Five roentgen-ray treatments; no return of cerebellar symptoms; death from spinal metastasis
24	P. B. B. H. 19775	F	9	3 mo.	Oct. 1, 1923, partial extirpation	3 mo.	Glioma	Two roentgen-ray treatments with temporary improvement; treatments not pursued
25	P. B. B. H. 21199	M	13	8 mo.	May 1, 1924, suboccipital decompression	6 mo.	Spongioblastoma	One roentgen-ray treatment
26	P. B. B. H. 21341	M	22	16 days	May 23, 1924, subtemporal decompression	Fatality	Neurocytoma	Acute onset following trauma; tumor an unexpected necropsy finding
27	P. B. B. H. 22167	M	6	3 yr.? 2 mo. rapid	Sept. 17, 1924, partial extirpation	Living	Glioma	Eight roentgen-ray treatments
28	P. B. B. H. 22601	M	9	24 mo.?	Nov. 25, 1924, fragmentary extirpation; removal of arch of atlas	Living	Glioma	One roentgen-ray treatment at P. B. B. Hospital; others elsewhere, number unknown
29	P. B. B. H. 22773	M	6	2 mo.	Dec. 11, 1924, extensive extirpation	Fatality	Neurocytoma	Tumor disclosed by incision of vermis

CASE 7.—*History.*—On Aug. 13, 1913, Mary M., aged 6½ years, a school girl, referred by Dr. William Sheehan of Salem, was admitted to the hospital, complaining of headache, vomiting, impaired vision and staggering gait. She had been a healthy child until the onset of her present symptoms, which were of only four months' duration. They were inaugurated by pressure symptoms, i.e., by severe headaches and attacks of vomiting. For two months there had been marked static instability with staggering. Her vision had been failing rapidly.

Examination.—This showed an emaciated, fretful and somewhat disoriented child with an enlarged head due to separation of the sutures. There was a bilateral choked disk with hemorrhages, a bilateral abducens palsy and no nystagmus. She was unable to walk without support. A marked incoordination of cerebellar type affected all extremities.

Course of Illness.—She became worse rapidly, and a few days after admission had a series of convulsive seizures of cerebellar type. These were accompanied by unconsciousness with marked retraction of the head and extensor rigidity of the extremities. In one of these attacks respiration ceased, and although artificial respiration was given until the ventricle could be punctured, the child did not recover. Permission was given for an examination of the brain, which was removed shortly after death. Complete necropsy was not performed.

Pathological Findings.—The brain was fixed with formalin before removal. It showed a marked hydrocephalus and a full cerebellum with a smooth midline tumor presenting between the herniated tonsils of the hemispheres (Fig. 1). A sagittal section (Fig. 2) disclosed a fairly well circumcised, median, spherical cerebellar tumor, overlying the fourth ventricle but not attached to it. The tumor gave the appearance of possibly arising from the tela choroidea. It blocked the iter, which was dilated to the size of a lead pencil.

Histologically the tumor was composed of an irregular mass of rounded cells (Fig. 3), with scanty cytoplasm and oval nuclei containing an abundant reticulum of chromatin. Intercellular fibrillar material was abundant. It contained a scanty reticulum of connective tissue and a few well developed neuroglia fibrillae, but consisted for the most part of numerous embryonic glia fibrillae (Fig. 4). These embryonic fibrillae stained with neither phosphotungstic acid hematoxylin, neutral ethyl violet orange G, nor Hortega's first variant, but were easily impregnated by the fourth variant. The centrosomes usually occurred as a single heavy granule, although diplosomes and rarely a triplosome were seen. No neurofibrillae could be found.

Comment.—The rather sudden, stormy onset of general pressure symptoms shown by this child is typical of most of the other cases in the series. The headache, vomiting and choked disk usually precede the signs indicating the location of the lesion. Indeed, the usual cerebellar tumor syndrome may be incomplete through the absence of a definite, sustained nystagmus. The inaugural pressure symptoms are unquestionably due to cerebrospinal fluid stasis, an inevitable and early complication of a tumor arising from the roof of the fourth ventricle. As the hydrocephalus forms, the cranial sutures may separate and more or less relieve the pressure symptoms, though rarely, even in young children, before the optic nerves have been seriously damaged.

The tissues in this case had been carefully studied by Professor Councilman, then pathologist to the hospital. The tumor was at first regarded as a neuroblastoma, but on further study, which revealed the presence of a few adult neuroglia fibrils which stained with phosphotungstic acid hematoxylin, the diagnosis was changed to glioma.

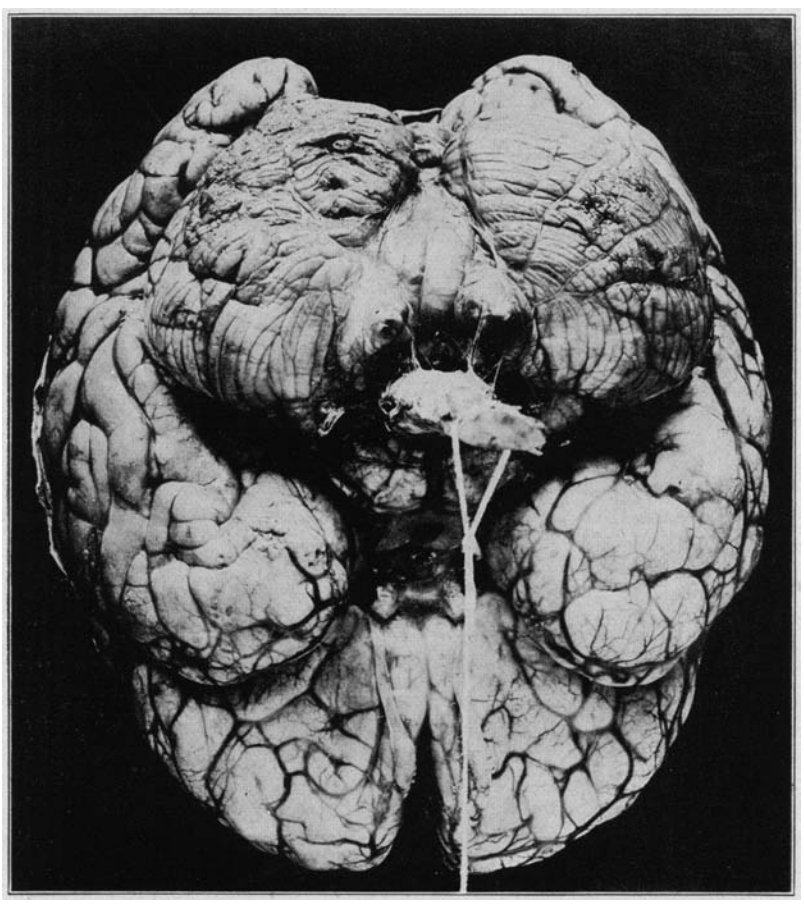

Fig. 1 (Case 7).—Mesial tumor presenting between cerebellar tonsils with brain stem being pulled away.

In the following case the symptoms were still more abrupt in their appearance. Scarcely eight weeks elapsed from the time of their onset to the child's death.

Rapid onset of cerebellar symptoms with hydrocephalus. Sudden death from respiratory failure. No operation. Necropsy. Midcerebellar medulloblastoma.

CASE 10.—*History.*—On Feb. *22*, 1915, Russel S., aged 15 years, a schoolboy, referred by Dr. J. H. Pratt, was admitted to the hospital, complaining of head-

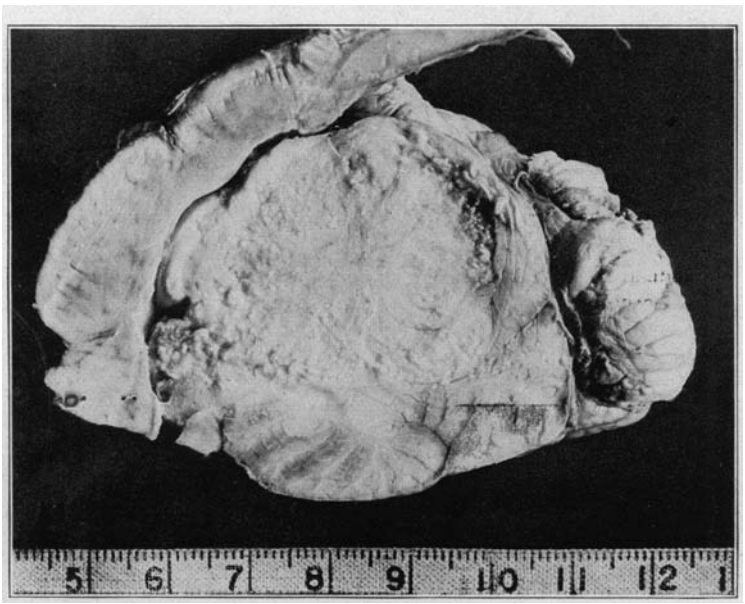

Fig. 2. (Case 7).—A sagittal section of the hind brain, showing the centrally situated lesion which has flattened the brain stem and widened the ventricle.

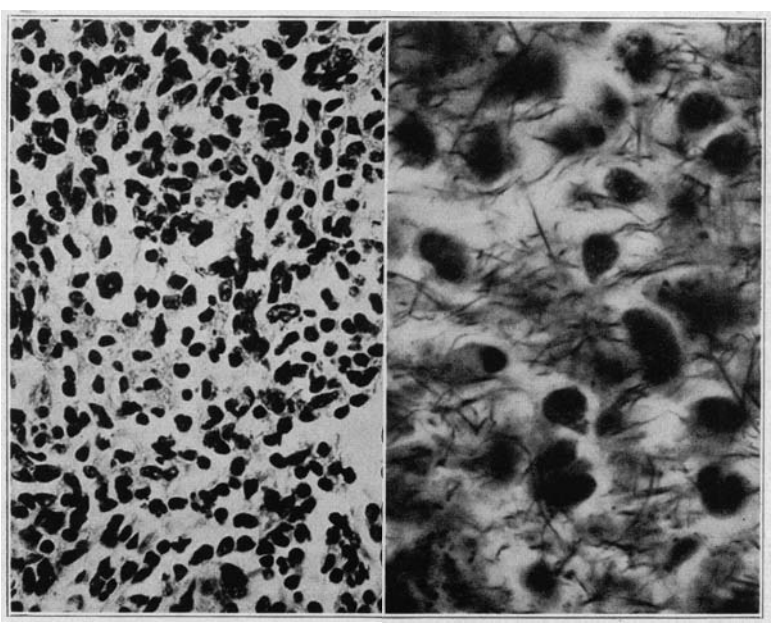

Fig. 3 (Case 7).—Structureless arrangement of cells; iron hematoxylin stain; × 300.

Fig. 4 (Case 7).—Processes of embryonic glia which do not stain with phosphotungstic acid hematoxylin; Hortega's fourth variant; × 850.

ache, vomiting, failing vision and staggering gait. The patient was said to have been in perfect health until Christmas, 1914, when he first complained of double vision and unsteadiness. Early in January he began to have periodic frontal headaches, which have persisted and which have usually been accompanied by vomiting. Since February 1 his vision had been failing, and his speech had been indistinct.

Examination.—This showed an emaciated boy who held his neck stiffly, with the head tilted to the right. There was a bilateral choked disk, with elevation of 8 diopters and extensive retinal hemorrhages. There was also paresis of the left abducens, nystagmus on looking to the right and left, dysarthria, and marked incoordination of cerebellar type of all the extremities. He was unable to stand unsupported.

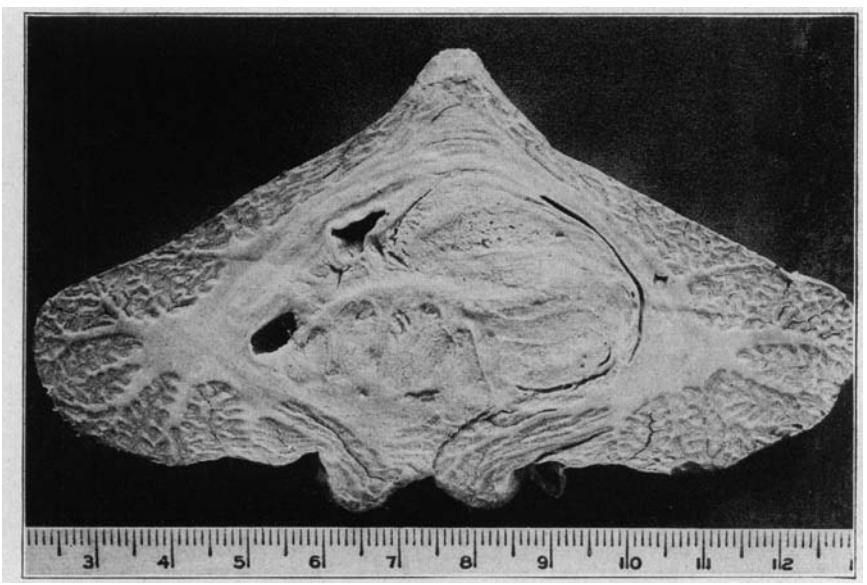

Fig. 5 (Case 10).—Cross section of cerebellum to show centrally placed tumor.

Course of Illness.—On the morning of Feb. 25, 1915, when about to be given an enema as part of his preparation for operation, he suddenly ceased breathing and died in a short time, in spite of artificial respiration. A complete necropsy was performed four and one-half hours postmortem.

Necropsy Findings.—No abnormalities were found elsewhere than in the brain. This had been fixed in 10 per cent. formalin. In addition to marked internal hydrocephalus, a fairly well circumscribed, midcerebellar tumor was disclosed (Fig. 5). At its periphery were two small cysts.

The tumor was studied and described in detail by Dr. Councilman, who pointed out among other things that the microscopic examination showed the tumor to be invading the cerebellar cortex; that islands of tumor cells were found far out in the molecular layer; and that at one place they appeared actually to be invading the leptomeninges. He observed that the general mass of the tumor consisted of closely packed, rounded or pear-shaped cells of

small size with oval nuclei containing a heavy reticulum of chromatin (Fig. 6); that mitotic division of the nuclei was common and that amitotic division was also present. Occasional neuroglia fibers were demonstrated by Mallory's stain, and a diagnosis of glioma of the cerebellum was made.

In addition, it is possible today to show that the intercellular material consists almost entirely of the processes of the neoplastic cells which are unipolar spongioblasts in various stages of formation (Fig. 7). The centrosome occurs as a single granule at the base of the protoplasmic process (Fig. 27). Occasionally adult neuroglia fibrillae can be differentiated in these processes. Here and there are necrotic areas around which the cells are collected in such a way as to form the sort of pseudo-epithelium which has been described by Saxer.

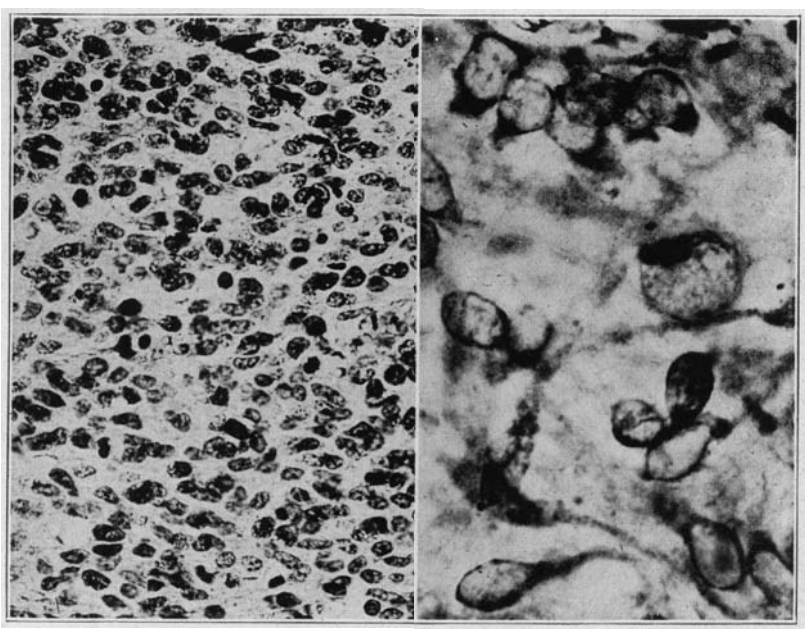

Fig. 6 (Case 10).—Structureless arrangement of tumor cells. Hematoxylin eosin stain; ×300.

Fig. 7 (Case 10).—Note shape of cells, particularly the pear-shaped cell with long process. Perdrau's method modified; ×850.

Comment.—A sagittal section through the cerebellum showed that the lesion occupied exactly the same midline relation to the fourth ventricle as shown in Figure 1. It had no attachment to the floor of the ventricle but appeared to lie above the tela; it extended upward as a roundish ball about 5 cm. in diameter; it occluded the iter which was greatly dilated. It is impossible of course to tell how long the tumor may have existed as a quiescent lesion; but this probably was not long, for an obstructive hydrocephalus was inevitable, and full-blown pressure symptoms must have followed quickly. As these tumors are likely to

project into and occlude the foramen magnum, a lumbar puncture under these circumstances is particularly dangerous. Opisthotenoid seizures with respiratory embarrassment or failure are the usual terminal clinical features of such a lesion.

The remaining twenty-seven patients with tumors in the series have all been subjected to operation, in some instances to successive operations, in what now appears to have been the vain hope that they might be enucleated. The temptation is great, for at first sight the lesion appears to be well encapsulated, and the cerebellum can be readily brushed away from its surface. The tumors, moreover, are fairly tough and can be handled easily, and, as stated above, they involve the roof only and not the floor of the ventricle.

In these twenty-seven cases there have been thirty-six operations, with eight postoperative fatalities, two of them after secondary operations. This gives a high mortality, though one which is perhaps not exceptionally so when one considers the situation of the lesion, the fact that the operation often necessitates the removal of the laminae of the atlas, and the fact that unless the procedure serves to reestablish the cerebrospinal circulation a bad matter may be made worse by the decompression.

The next case is an example of an operative fatality following the attempted removal of one of these tumors.

A six months' history of a midcerebellar tumor. Partial extirpation. Postoperative fatality. Necropsy. Medulloblastoma.

CASE 3.—*History.*—On July 9, 1909, Blanche R., aged 9, a schoolgirl, was admitted to the Johns Hopkins Hospital, complaining of headaches, vomiting and instability. A normal, bright child, she had enjoyed almost perfect health until her present illness. This began in January, 1909, when she complained of occasional frontal headaches, and it was noticed that she was unsteady on her feet and had a habit of rolling her head backward. The headaches soon became associated with spells of vomiting. These symptoms increased progressively in severity until by April she was unable to walk alone, and her vision had become impaired. At about the same time an internal squint of the right eye was noticed, and a few weeks ago of the left, together with a facial weakness on the same side. She had also had tinnitus in the left ear.

Examination.—On admission she had a bilateral choked disk progressing to atrophy, a cracked-pot sound on percussion of the skull, with separation of the sutures, a bilateral abducens palsy, and paresis of the left facial nerve (Fig. 8). In addition there was marked incoordination of cerebellar type of all four extremities; she was unable to stand or walk alone.

Course of Illness.—At operation, on June 13, 1909, a suboccipital exploration revealed a large solid reddish tumor in the center of the cerebellum. A mass the size of a pigeon's egg was enucleated, leaving a raw, blood stained pocket. The child endured operation poorly, and died three hours later. Necropsy was restricted to an examination of the brain, which was removed after formalin fixation in situ.

Pathology.—A block of the tumor which had been removed at operation and immediately fixed in Zenker's fluid was forwarded to Dr. Mallory for a histologic report. Recognizing its resemblance to the tumors which Dr. Homer Wright was then studying, the case was included as Case 12 in Dr. Wright's series of neuroblastomas, with the bare statement that "the tumor shows the characteristic ball-like arrangement of cells and fibrils." No other histologic study of this tumor seems to have been made (Fig. 9).

The Zenker-fixed specimen removed at operation is available for examination, and the brain and the remnant of tumor which showed on coronal section (Fig. 10), as a discrete, rounded, centrally placed mass, 4.5 x 3 cm., overlying the fourth ventricle, together with some clotted blood.

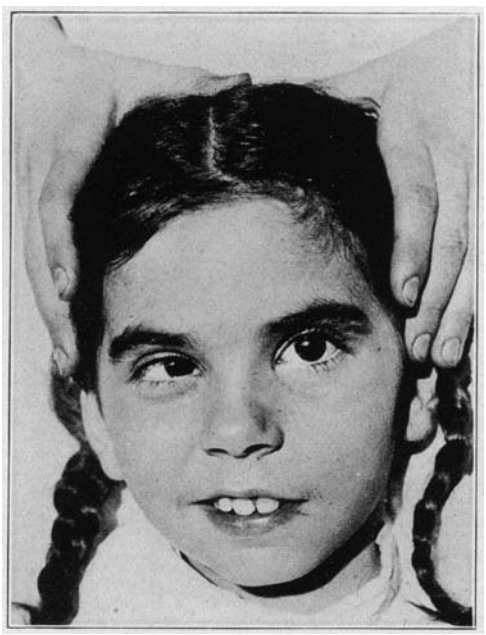

Fig. 8 (Case 3).—Left facial and abducens palsies.

A restudy of the tumor showed it to be composed of a mass of cells without any particularly distinctive architectural arrangement (Fig. 11). The nuclei were round or oval, with an abundant network of chromatin. Cytoplasm was scanty. No centrosomes were seen. Occasional mitotic figures were found. Blood vessels were large but not very numerous. There was a small amount of intercellular fibrillar material, consisting of reticulum, embryonic glia (Fig. 12) and some well developed neuroglia fibrillae. Collagen was restricted to the walls of the blood vessels. Even in the formalin-fixed material no neurofibrillae could be demonstrated.

This case has obscurely found its way into the literature not only in connection with Dr. Wright's report, but also in regard to another matter once made the subject of study by the senior author: namely,

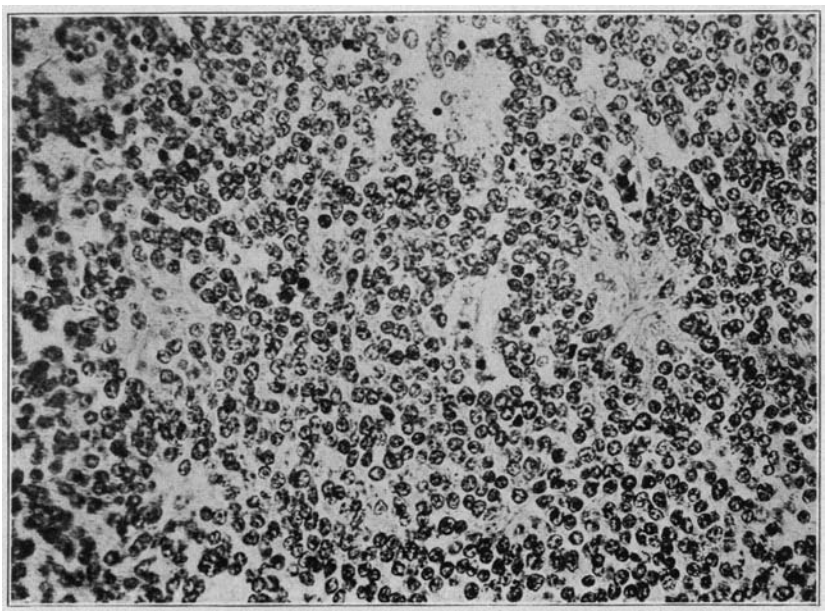

Fig. 9 (Case 3).—Ball-like arrangement of cells. Phosphotungstic acid hematoxylin stain; × 300.

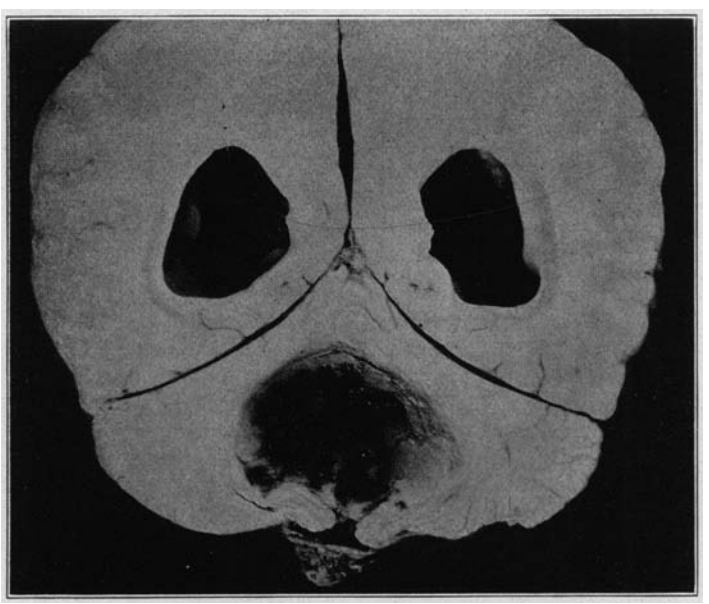

Fig. 10 (Case 3).—Centrally situated tumor.

in connection with internal squint as a false localizing sign of tumor.[7] This case happened to be one of those which was reported at that time as an example of strangulation of the abducentes (Fig. 13). As a matter of fact, an abducens palsy, often bilateral, is of common occurrence in many cerebellar tumors, possibly more common, it would appear, in these midline tumors than in any others. Indeed, it is the one outstanding symptom in addition to the general pressure symptoms brought about by the hydrocephalus and the instability and cerebellar ataxia which the patients show. Whether the squint is actually due to such

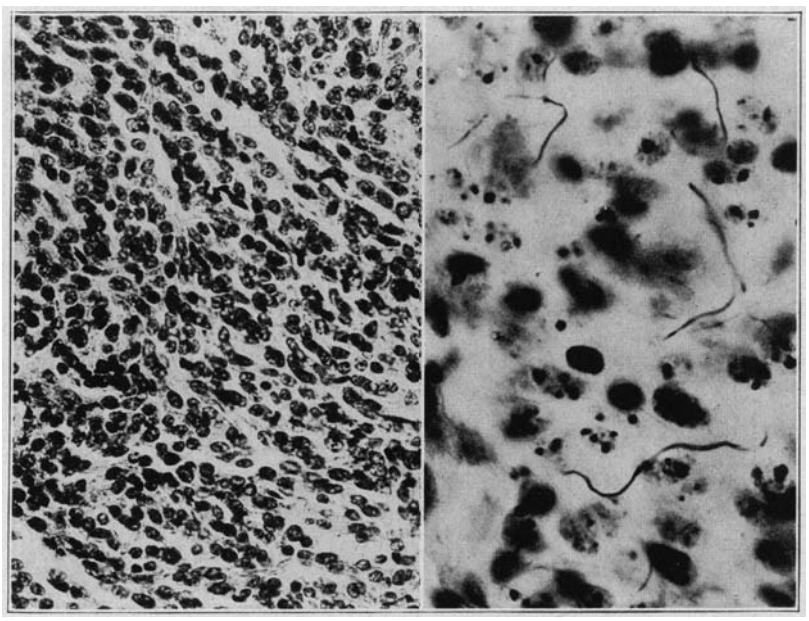

Fig. 11 (Case 3).—General appearance of the tumor on section. Hematoxylin eosin stain; × 300.

Fig. 12 (Case 3).—Processes of embryonic glia demonstrated by Hortega's fourth variant; × 850.

a mechanical cause cannot be definitely asserted. The fact that in this child there was a facial palsy on one side would perhaps be a further argument in favor of the direct implication by pressure of the nuclei for the sixth and seventh nerves.

In the series of twenty-nine cases, there has been only one in which a widespread "sarcomatosis" of the meninges has been observed. The

7. Cushing, H.: Strangulation of the Nervi Abducentes by Lateral Branches of the Basilar Artery in Cases of Brain Tumor, Brain **33**:204-235 (Oct.) 1910.

case happens to be another of those in the Baltimore records of the senior author. It is as follows:

Median cerebellar medulloblastoma with wide dissemination in the leptomeningeal spaces. Original pathologic diagnosis, meningeal sarcoma. Fatality at second operation. Necropsy.

CASE 5.—*History.*—On March 16, 1910, George B., aged 7, a schoolboy, was admitted to the Johns Hopkins Hospital, complaining of headache, double vision, vomiting and unsteady gait. He had been in good health until early in January, 1910, when he had his first symptoms of suboccipital pain and vomiting. By February, double vision was noted. He rapidly became worse. For the past month his gait had been unsteady, and he had vomited frequently. Three

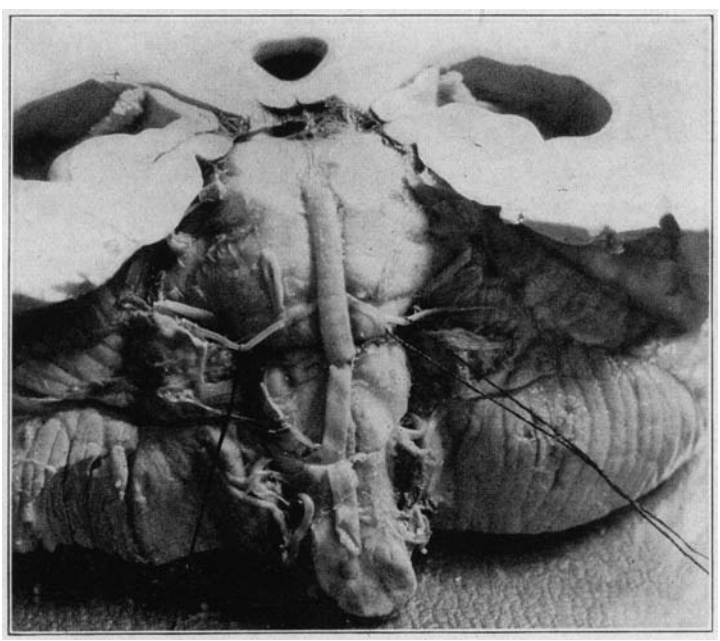

Fig. 13 (Case 3).—Strangulation of the abducens produced by lateral branches (drawn away by threads) of the basilar artery.

weeks prior to admission, he had an "attack" characterized by retraction of the head, Cheyne-Stokes respiration and unconsciousness which lasted for three days. Tuberculous meningitis was suspected. A similar attack occurred a few days before his entrance to the hospital.

Examination.—On admission he was stuporous and his head was retracted. Percussion of the skull gave a cracked pot sound; the eyes showed a bilateral choked disk with elevation of 7 diopters. There was a definite Kernig sign; knee reflexes were not obtainable; gait and station were impossible to test; there was no nystagmus.

Course of Illness.—A bilateral cerebellar exploration was performed on March 21, 1910. An extremely tense cerebellum was exposed, on the surface of which were two discrete nodules of a soft, grayish tumor. One was removed

for study. It was necessary to puncture the lateral ventricle to diminish tension sufficiently to close the wound. On examination the tissue showed what was taken to be an invasion of the meninges by a small round cell sarcoma.

The child made a temporary marked improvement and was discharged. He continued to do fairly well until July when he had a severe cerebellar "fit" similar to those preceding his first operation, and he was brought back to the hospital for observation. An operation seemed to offer the only hope of giving further relief. On July 19, 1910, a reexploration was made of the cerebellar region, with partial extirpation of a lobular, soft, apparently encapsulated tumor

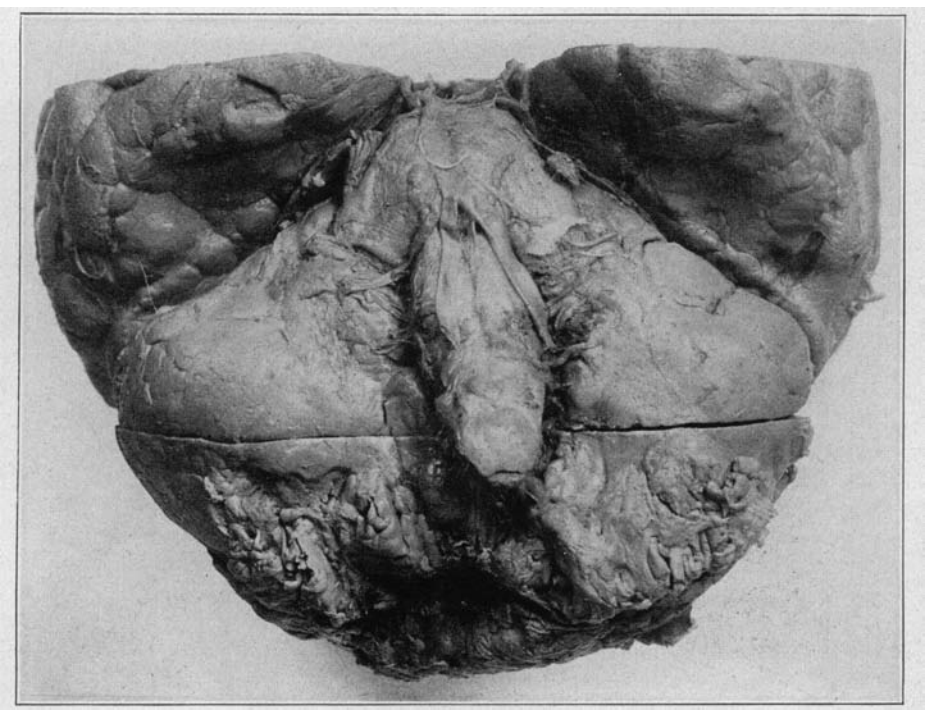

Fig. 14 (Case 5).—Tumor extension throughout the cerebellar leptomeninges.

from the center of the cerebellum. The tumor proved to be of great size, and several large masses of it were removed. The child died not long after the termination of the operation.

Necropsy Findings.—The postmortem examination was limited to the examination of the brain which was fixed by formalin injection before removal. It showed a marked hydrocephalus. It was evident that the intracerebellar portion of the tumor had been almost completely removed, but the growth has spread in the meningeal spaces solidly over the cerebellum (Fig. 14), and in patches over the cerebral hemispheres, where it was visible as flat nodules in the sulci under the arachnoid membrane (Fig. 15). The spinal cord was not examined.

There was available for reexamination some of the material removed at operation and fixed in Zenker's fluid, and the brain fixed in 10 per cent. formalin. The cerebellar tumor was composed of an irregular mass of cells with oval nuclei containing an abundant reticulum of chromatin (Fig. 16). The cytoplasm of these cells was fairly abundant, and there was a large amount of intercellular fibrillar material, consisting of reticulum, collagen, protoplasmic processes of the cells, and numerous adult neuroglia fibrillae which stained with phosphotungstic acid hematoxylin (Fig. 17).

In the nodules of tumor over the surface of the brain the cells were almost similar, but there were more collagen fibers and no neuroglia fibrillae. Mitotic figures were common.

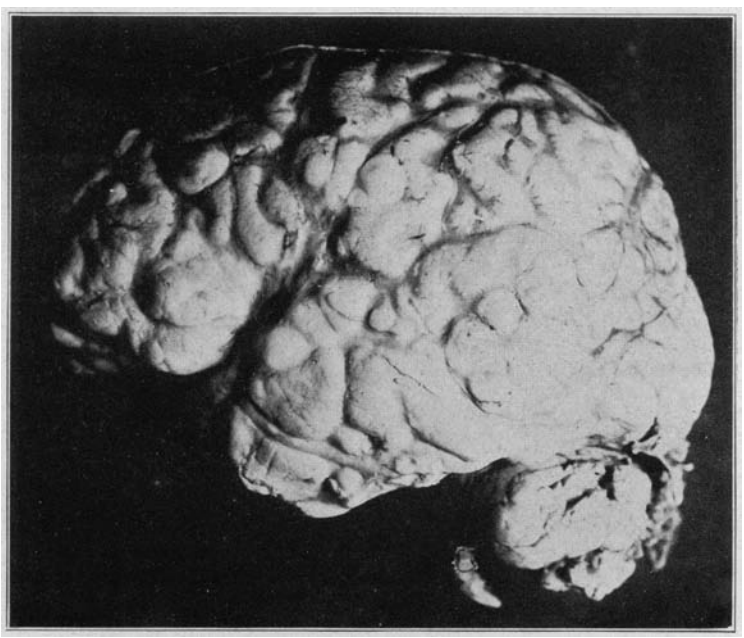

Fig. 15 (Case 5).—Nodules of tumor through the leptomeningeal spaces over the cerebrum.

The midcerebellar tumor in this case was of precisely the same character as that in all the others, but it must be admitted that the meningeal nodules, examined alone, might easily give the impression of a sarcomatous invasion. If we had known as much as we do today about these conditions, it is improbable that this child would have been subjected to his secondary and what proved to be his fatal operation. But there can be no doubt of the marked temporary improvement for three or four months after the first operation, which amounted to nothing more than a decompression.

Attention may be called to the fact that the meninges in this case were found to be "infected" by the tumor when the cerebellum was

first exposed, so that the spread of the lesion into the leptomeningeal spaces was not due to the operation. As a matter of fact, such an occurrence seems to be less common than one might expect in consideration of the active cell division which characterizes these lesions. Of the twenty-nine cases, excluding this particular one, there have been only three in which it was assumed that the spinal meninges had become "infected" by a tumor implant; and in one of them such a metastasis was verified by a laminectomy performed elsewhere.[8]

We have so far cited two examples of the tumors in question which proved fatal without operative intervention; a case in which operative

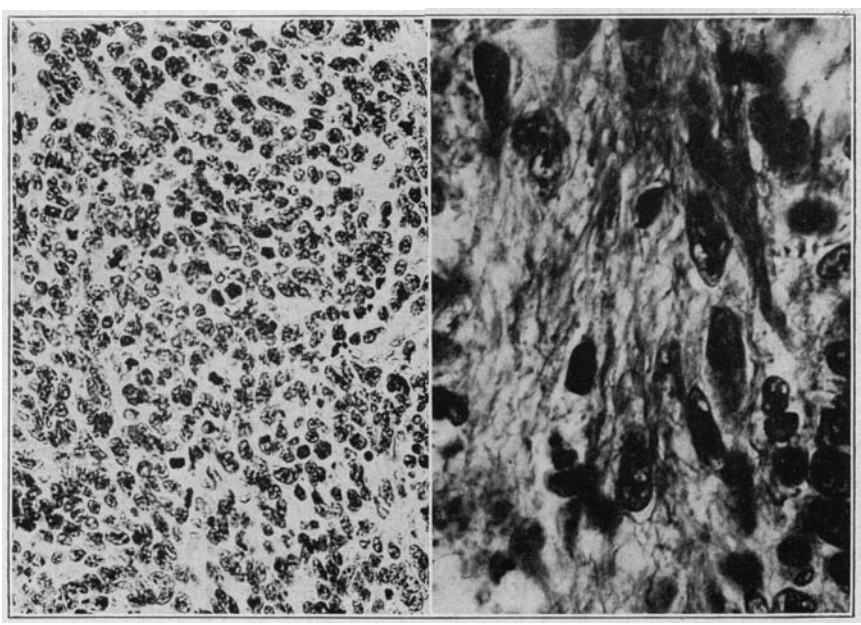

Fig. 16 (Case 5).—Usual structureless arrangement of cells. Phosphotungstic acid hematoxylin stain; × 850.

Fig. 17 (Case 5).—Adult neuroglial fibrillae which stain with phosphotungstic acid hematoxylin; × 850.

intervention led to a fatality, and a case which was characterized by the invasion of the meninges by the tumor. The following case will show that the survival period after adequate decompression and partial enucleation of the tumor with immediate recovery from the operation may nevertheless be brief. The story is of less interest from a clinical than from a pathologic standpoint. Though an early case in the series, the operative tissues happened to have been fixed in formalin, and the

8. Elsberg, Charles A.: Tumors of the Spinal Cord, New York, Paul Hoeber, 1925, p. 161, Case LIV.

tumor proved to be one in which there was a larger amount of the internuclear fibrillar material than usual. It is chiefly for this reason that the case has been selected for report.

Characteristic symptoms of five months' duration. Temporary improvement following partial extirpation of tumor. Death two months later. No necropsy.

CASE 9.—*History.*—On Dec. 6, 1914, Louis E., a schoolboy, aged 8 years, referred by Dr. E. H. Beall of Fort Worth, Texas, was admitted with the complaint of headache, vomiting, unsteadiness and incontinence. With the exception of occasional slight headaches, he had always been well until July, 1914, when his major symptoms appeared with the usual abruptness—frontal headache, projectile vomiting, unsteadiness, dizziness and diplopia. These symptoms gradually increased in severity. He was given a course of antisyphilitic treatment, with apparent improvement. In September, it was first noticed that he had some incoordination of his upper extremities. In November, slight nystagmus and optic neuritis were first observed. For the past two weeks, he had been incontinent of urine.

Examination.—On admission, he had wide pupils, a bilateral choked disk advancing to atrophy, nystagmus on looking to the right and left, a divergent strabismus, dysarthria, incoordination of all the extremities of cerebellar type, more marked on the left side. He was too ill to test gait and station.

Course of Illness.—On Dec. 14, 1914, at operation the usual bilateral suboccipital exposure, after ventricular puncture, revealed a full cerebellum with marked foraminal herniation but no evidence of tumor. A transverse incision through the left hemisphere came down on a firm, dark red tumor situated in the middle of the cerebellum. Though vascular, it was apparently encapsulated and thought to be enucleable. A mass about the size of a bantam's egg was extirpated. The child made an excellent recovery from this operation, with relief from headache and vomiting, subsidence of choked disk and improvement in ataxia, so that he was able to walk about with slight assistance. He was discharged, Jan. 7, 1915. The improvement was brief. A month after his return home he became worse again, had respiratory and deglutitory difficulties and died on Feb. 21, 1915. No postmortem examination was made.

Pathologic Examination.—The material removed at operation was fixed immediately in 10 per cent. formalin. Dr. Councilman, though recognizing the resemblance of the tumor to the preceding examples in the series, called special attention to the similarity with another fourth ventricle tumor which proved to be an ependymoma. The demonstration of occasional adult glia fibrils caused him to place the tumor in the glioma group.

As in the other cases in the series, the tumor was composed of an irregular mass of cells (Fig. 18), with rather numerous, thin-walled blood vessels. There was perhaps a greater abundance of intercellular fibrillar material than usual; it consisted of some connective tissue reticulum, a very little collagen about the larger blood vessels, a few well-differentiated adult neuroglia fibrillae (Fig. 19), and numerous embryonic neuroglia processes which were demonstrable only by Hortega's fourth variant (Fig. 20). No neurofibrillae were to be found. A few nuclei of dumb bell shape were seen, presumably dividing by amitosis. Mitotic nuclear figures were common.

The period of improvement in this case was of unusually short duration, shorter indeed than in any other case in the series in which

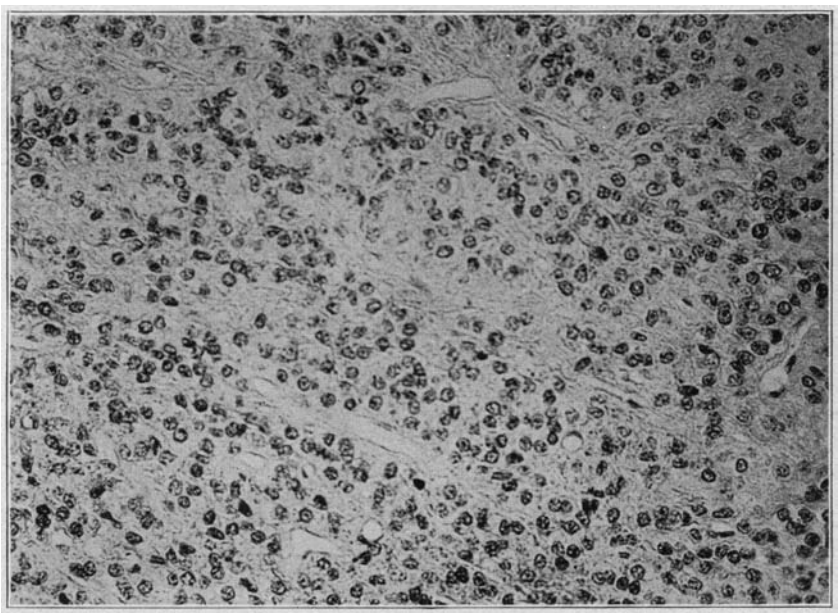

Fig. 18 (Case 9).—Abundant internuclear material which does not stain with phosphotungstic acid hematoxylin; × 300.

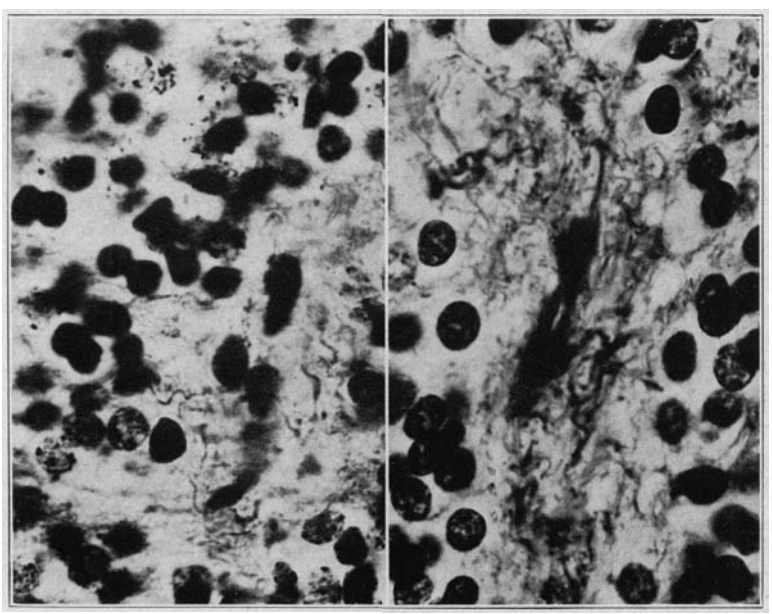

Fig. 19 (Case 9).—Adult neuroglial fibrillae shown by Hortega's first variant; × 850.

Fig. 20 (Case 9).—Embryonic glial processes shown by Hortega's fourth variant; × 850.

the patient survived operation, as can be seen from the table. In one case, the first in the Brigham Hospital list (Case 6), the patient had an extraordinarily long survival period, twenty-one months, from the time of the first operation, which amounted merely to a decompression. At two subsequent operations, the tumor, which the decompression had permitted to attain an enormous size, was radically extirpated. These repeatedly successful operations doubtless account for the long survival period.

It will be seen also that the next three patients that were operated on (Cases 11, 12 and 13) had survival periods of nine, ten and sixteen months, respectively, although in the last of these the operation amounted to little more than a decompression with the removal of a fragment of tumor for histologic examination.

As the table makes evident, radiation was first employed as a supplementary measure to the operation in Case 14, and immediately the survival periods began to lengthen. Radiation, however, has not accomplished all that might be desired, although the results have on the whole been much more favorable than by operation alone. The history of the longest survival—a story not yet completed—is as follows:

Midcerebellar medulloblastoma arising from above the fourth ventricle. Operation with subsequent radiation and survival for more than four years.

CASE 17.—*History.*—On Feb. 9, 1921, Jack H., aged 6 years, a schoolboy, referred by Dr. E. Koplik of New York City, was admitted to the hospital with the complaint of headache, vomiting, crossed eyes and unsteadiness.

In July, 1919, having previously been in good health, he began to have attacks of vomiting. These were treated as gastric attacks. There were no headaches. In May, 1920, he complained of double vision. Two months later, he had his first severe frontal headache, which lasted for two days. Similar bad headaches recurred, and soon were practically constant. In some of the last attacks he was unconscious for a few minutes, with retracted head and rigid body. Some unsteadiness seems to have been present for about two years. The parents thought the boy was clumsy. For the past three months there had been definite staggering with inability to walk alone.

Examination.—On admission the patient was a bright boy with an enlarged head which gave a cracked pot sound on percussion. A bilateral choked disk was present, with an elevation of 4 diopters, hemorrhages and considerable secondary atrophy. There was paresis of the left external rectus muscle, marked nystagmus on looking to either side, and incoordination of cerebellar type involving all extremities. He was able to take a few steps, but his gait was most unsteady.

Course of Illness.—On Feb. 14, 1921, the usual bilateral suboccipital exploration was made, revealing a median cerebellar tumor projecting down inside the posterior cistern through the foramen magnum. In order to expose the lower margin of this projection, it was necessary to remove the posterior arch of the atlas and to carry the dural incision down to the axis. The appearance is roughly shown in the accompanying sketch made at the time (Fig. 21).

It was hoped that the tumor might be tilted upward, but it was found that the growth could not be separated from the medulla in the region of the calamus because of the presence of a large artery which crossed this part of the lesion. Several portions of the soft tumor were removed for histologic study; the bleeding was checked and the wound closed.

The boy recovered promptly. Headache and vomiting ceased, and he was discharged on March 11, 1921, in excellent condition, with few traces of his former symptoms. He subsequently received about five roentgen-ray treatments. He returned on July 16, 1923, at which time he showed no symptoms of any cerebellar disturbance. He remained free from symptoms for four years. He attended school, engaged in sports and was apparently normal in all respects. He reentered the hospital on March 9, 1925, four years after the operation, with slight evidence of the return of his former symptoms—some vomiting and headache but no cerebellar signs (Fig. 22)."

Pathologic Description.—The material removed at operation was fixed in Zenker's fluid, and consequently impregnation methods for embryonic glia and neurofibrillae were precluded. The tumor was diagnosed at the time as a neurocytoma.

A reexamination showed that the growth consisted of a disorderly mass of cells with oval nuclei almost similar to those described in the other cases (Fig. 23). The nuclei had abundant chromatin. There was considerable intercellular material, though less than in the preceding case, consisting for the most part of thick processes of the cells and occasional well developed adult neuroglia fibrillae (Fig. 24). Connective tissue was confined to the walls of rare blood vessels. The centrosomes could not be seen. Mitotic figures were frequent. It was impossible to stain for neurofibrillae, but no cells resembling neuroblasts were to be found.

Comment.—The case is an example of what may be accomplished for even such serious lesions as those which comprise this series. A new growth could hardly be situated in a position more dangerous to life, and when it is a rapidly growing lesion, as are the medulloblastomas, the

9. This case is important enough to deserve this additional footnote. On readmission, after a four year interval, one would hardly have believed that there had ever been a cerebellar operation. The occipital bone had been almost entirely reformed, and there was no suboccipital protrusion. The patient had no evident pressure symptoms other than slight subjective discomforts, and no choked disk. There were practically no cerebellar signs. Nevertheless, under the belief that there must have been a reactivation of the quiescent growth, on March 23 he was given a deep therapeutic roentgenization of the cerebellum. A few hours later, he began to have severe headaches and vomited, and within twelve hours had become stuporous. His stupor increased, with a slow pulse and Cheyne-Stokes respiration. As a life-saving measure, under local anesthesia, the old cerebellar flaps were reflected, the new-formed bone removed, and a huge, softened median cerebellar growth was easily detached. This exposed the greatly widened floor of the fourth ventricle, and one could look into the distended iter from which fluid escaped in abundance. The child had a very close call from a postoperative hyperthermia, but from this he recovered, had a good convalescence, and was discharged. It is hoped that he will have at least another four-year period of relief, if indeed the growth may not have been completely destroyed by this radiation.

fact that one should occasionally be able to prolong life and at the same time make it worth living by any therapeutic measure whatsoever is enough to encourage us to persist in our efforts. It is probable that with our present-day knowledge of the symptomatology of these lesions, of their pathologic nature, of the limits to which the operation should be confined, namely, largely to decompressive measures, and of the beneficial

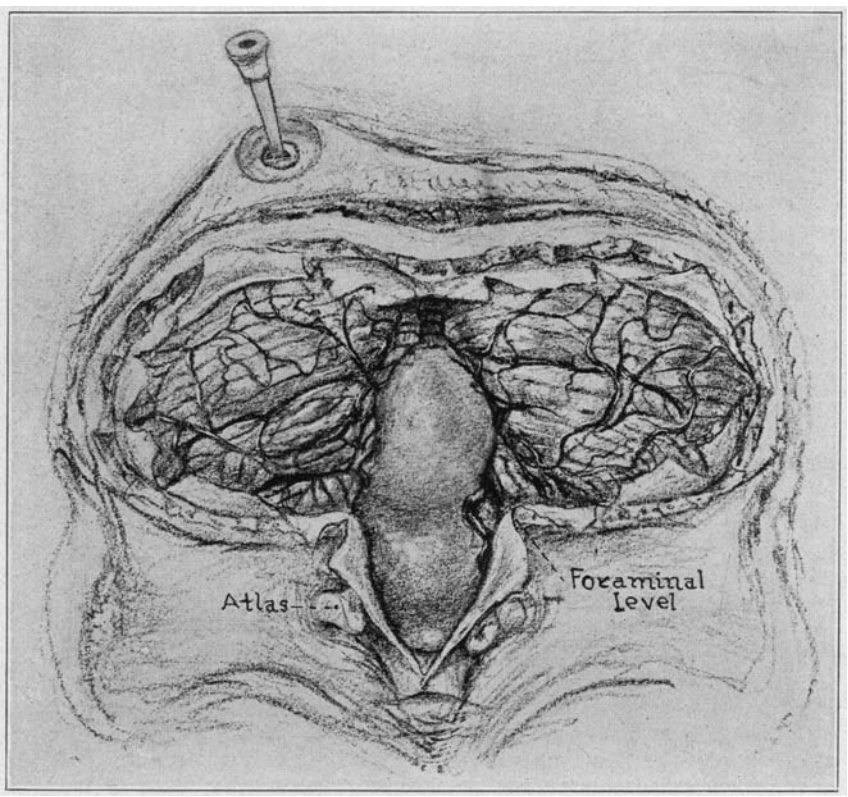

Fig. 21 (Case 17).—General appearance and situation of tumor as exposed at operation.

effects of radiation, that future series of cases in the same or other hands will show much more encouraging results.

CLINICAL SYNDROME

The syndrome of these cases might be easily forecast from a knowledge of the primary site of the tumor and of its histologic nature. Taking the case histories as a whole, the inaugural symptoms in most instances were those of increased intracranial tension, the evidence of which was likely to be abrupt and to have been present for comparatively

few months before the patient's admission to the hospital. It is true that the histories occasionally tell of an occasional headache of obscure origin, usually attributed to some gastric upset, for a year or so before, but the usual story is one which can probably be ascribed to a comparatively abrupt and more or less complete block of the cerebrospinal fluid with internal hydrocephalus. These symptoms are headache, projectile vomiting and the rapid appearance of choked disk. Since the patient is usually preadolescent, a separation of the cranial sutures, which gives the characteristic cracked pot-sound to the skull on percussion, is likely to be present.[10]

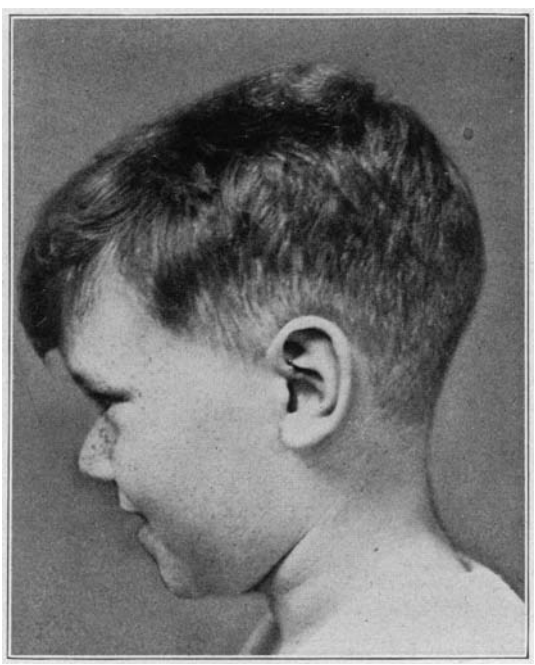

Fig. 22 (Case 17).—Patient after four years, showing absence of any suboccipital bulging.

In the general run of cases, the symptoms of primary pressure which may be properly ascribed to the hydrocephalus may overshadow

10. One case in the series (Case 26) shows, nevertheless, that a tumor of considerable size may be completely latent. The patient was a young man, aged 22, who supposedly had had no symptoms of any intracranial trouble until sixteen days before his admission to the hospital, when he had been kicked on the head in a football scrimmage. He was supposed to have a post-traumatic lesion; a lumbar puncture was performed, and subsequently a subtemporal decompression, which apparently precipitated his death. A medico-legal examination disclosed an entirely unsuspected midcerebellar medulloblastoma of characteristic histology.

the signs of cerebellar involvement. However, there is almost always a history of a staggering gait, and by the time of the patient's hospital admission, a full-blown cerebellar syndrome is usually apparent. The ataxia is likely to be more evident in the lower extremities than in the upper, and most of the children were unable to stand alone or to take steps without assistance. In several of them there had been a history of cerebellar seizures with retraction of the head, respiratory difficulty and other symptoms which suggested a basilar meningitis.

In the discussion of one of the cases attention has been called to the fact that nystagmus has been an inconspicuous feature of the cerebellar

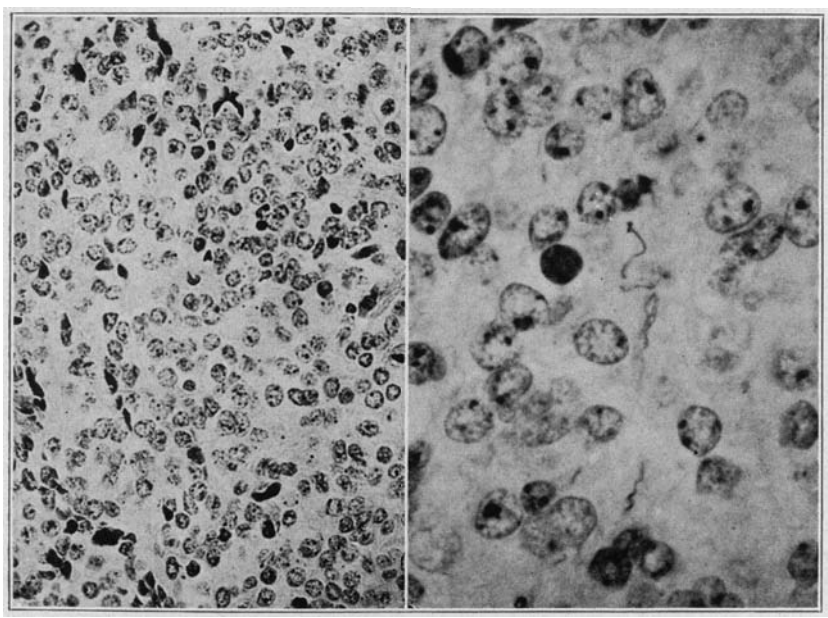

Fig. 23 (Case 17).—A section of tumor stained with methylene blue eosin; × 300.

Fig. 24 (Case 17).—Adult neuroglial fibrillae shown by neutral ethyl violet orange G. stain; × 850.

syndrome, as might possibly be expected from the midline position. However, diplopia has almost always been present, and in perhaps more than the usual number of cerebellar cases there has been a bilateral abducens palsy. In three or four cases, also, there has been a slight weakness of the face on one side.

The average age in the twenty-nine cases is 10 years. Five cases occurred when the patients were in the twenties; with these exceptions all were below 15 years. Twenty out of the twenty-nine cases occurred during the first decade of life.

THE PATHOLOGY OF THE LESION

As stated, in all the cases, the tumor seems to have originated over the roof of the fourth ventricle and to have developed as a central intracerebellar lesion. The lesions have appeared macroscopically both at operation and at necropsy to be fairly well circumscribed, though histologic study invariably has shown invasion of the surrounding cerebellar tissue. When the neoplasm appears on the surface (Fig. 1), it first becomes evident between the tonsils of the cerebellum, and experience at the operating table (Fig. 21) has shown that the growth is particularly likely to crowd its way downward through the foramen magnum. The fourth ventricle of course is greatly enlarged and deformed, and an unattached tongue of the tumor in one case extended even through the dilated iter into the third ventricle. In four instances, the tumor apparently had "infected" the subarachnoid spaces, three times forming metastases in the spinal region and once (Case 5) spreading widely through the leptomeninges over the base of the cerebellum and even over the surfaces of the cerebral hemispheres.

Histologically, these tumors are composed of rounded or pear-shaped, sometimes spindle-shaped cells, with scanty cytoplasm and big oval nuclei containing an abundant network of chromatin. On low magnification, the cells as a rule appear as a loose structureless mass, but the nuclei occasionally show architectural disposition and may form pseudo-rosets (Fig. 25) or lie in strands suggesting the arrangement of nuclei in a spindle cell sarcoma. Again, they may lie grouped around irregular spaces and acquire a sort of palisade arrangement (Fig. 26). These variations, which may be seen in different parts of the tumor, are of no essential importance.

From one or sometimes from both poles of the cells, there emerges an elongated process at the base of which a centrosome, surrounded by a clear halo, may often be seen. This usually is a single granule (Fig. 27), though occasionally it shows as a diplosome. These processes make up the bulk of the internuclear material, in which occasional thin-walled blood vessels may be found; and such delicate connective tissue as is demonstrable by Perdrau's method is usually confined to their walls (Fig. 28). Such variations as exist in the gross microscopic picture are consequently due to the relative abundance and arrangement of the cell processes rather than to the presence of any connective tissue stroma.

That the internuclear material is composed largely of the processes of embryonic glia cells can be shown by its ready impregnation with Achúcarro's tannic silver method (Fig. 29), as well as with Hortega's fourth variant of this method when the material has been suitably fixed. In material fixed in Zenker's fluid occasional adult neuroglia fibrillae can

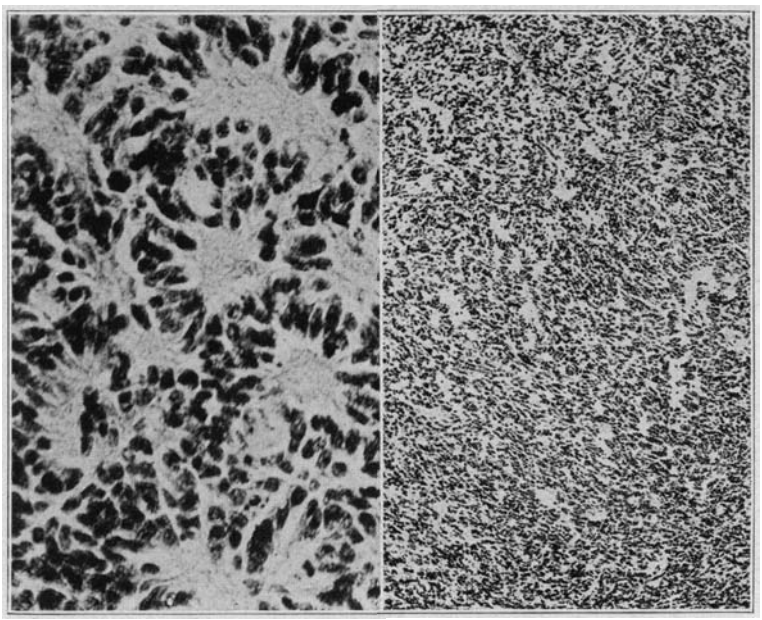

Fig. 25 (Case 18).—Ball-like pseudorosets of the medulloblastoma. Hematoxylin and eosin stain; × 600.

Fig. 26 (Case 18).—Showing irregular areas free of nuclei, the nuclei forming a sort of palisade around them. Neutral ethyl violet-orange G. stain; × 80.

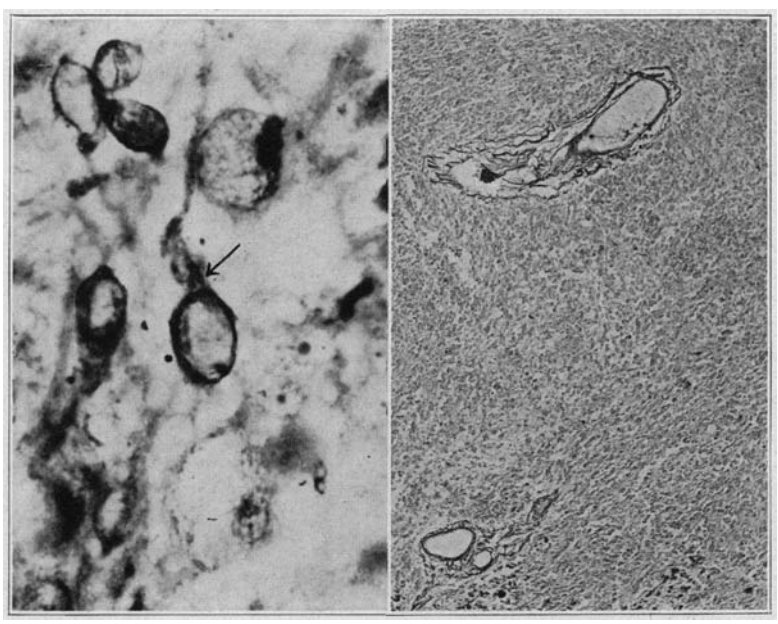

Fig. 27 (Case 10).—Unipolar spongioblast with single centrosome, at base of process, surrounded by clear halo. Perdrau's method, modified; × 850.

Fig. 28 (Case 12).—Usual arrangement of connective tissue in these tumors, surrounding small blood vessels. Perdrau's method; × 80.

be stained by the usual methods. No neurofibrillae are demonstrable by any of the appropriate stains, whatever the fixation.

ORIGIN AND NATURE OF THE TUMOR CELLS

Many of the cells are so undifferentiated that their nature is not evident from their microscopic structure. If of ectodermal origin, they must be akin to the "indifferenten Zellen" of Schaper,[11] or as we prefer to call them, medulloblasts. It is well known that the cells forming the cerebellum migrate in an extraordinary way during embryonic life, and it would seem to be not improbable that in this situation groups of cells might become isolated and retarded in their development.

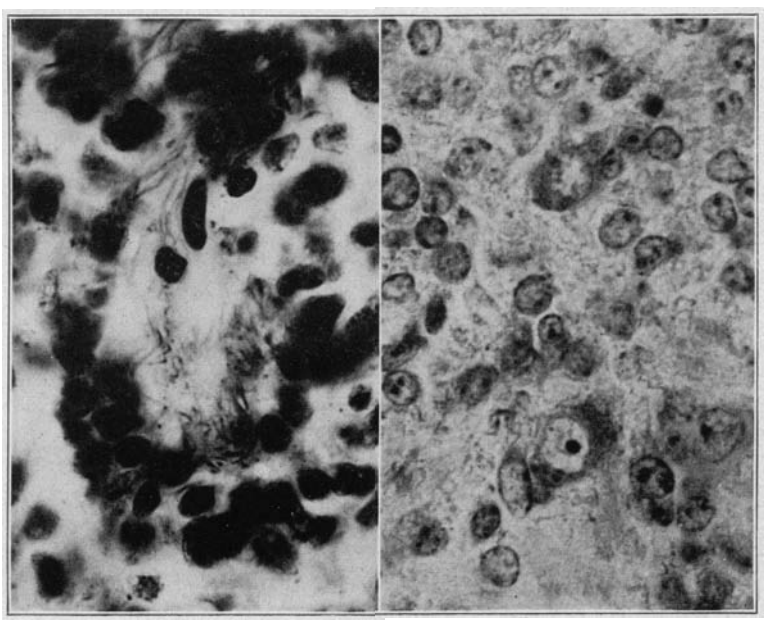

Fig. 29 (Case 12).—Typical ball of cells, showing delicate fibrillae impregnated by Achúcarro's tannic silver method; × 850.

Fig. 30 (Case 19).—To show what are supposed to be neuroblasts, with large nuclei containing a heavy nucleolus. Methylene blue-eosin stain; × 850.

Should these isolated cellular groups differentiate, a heterotopic malformation would result. Pfleger[12] found such heterotoptic cellular groups in the region of the fourth ventricle in seventy-five out of 400 supposedly normal cerebella. If such an isolated and retarded group of

11. Schaper, A.: Die Frühesten Differenzirungsvorgänge im Centralnervensystem, Arch. f. Entwklngsmechn. **5**:81, 1897.

12. Pfleger: Centralbl. f. d. med. Wissensch., 1880, No. 26, p. 468.

undifferentiated cells should undergo a neoplastic transformation, just such a tumor as we have described might be expected to result.

Schaper believed his indifferent cells capable of differentiation either into neuroblasts or spongioblasts. In one restricted area in one of our tumors, cells were found which showed the characteristics of neuroblasts. The tissue in this case had been fixed in Zenker's fluid so that it was impossible to obtain positive evidence of this fact by impregnation with silver. Nevertheless, the large circular nuclei, containing no scattered granules of chromatin and a single heavy nucleolus surrounded by heavily stained cytoplasm, can scarcely be interpreted otherwise than as belonging to neuroblasts (Fig. 30). An attempt to stain tigroid substance in their cytoplasm with the methylene blue-erythrosin method of Held was not successful.

Although a few of the neoplastic cells are, therefore, neuroblasts, many more are spongioblasts, their structure and staining reactions being identical with those of the unipolar spongioblasts of the developing central nervous system, as the preceding descriptions show. Their spongioblastic nature is further evidenced by the fact that neuroglia fibrillae are occasionally differentiated within them, as is shown by the ordinary staining methods for such fibrillae. The differentiation of adult neuroglia fibrillae seems to be accompanied by other changes in the cell, for they seem to come from the neighborhood of smaller, more heavily stained nuclei, while the more delicate embryonic processes come from larger nuclei which are more vesicular. An attempt to show these differences has been made in Figure 31. In some of these more differentiated cells, the development has gone so far that when impregnated by Cajal's gold sublimate method they appear as typical astrocytes. It might be supposed that such astrocytes as are shown in Figure 32, from one of these tumors, were merely inclusions of normal tissue cells in the new growth. This supposition seems untenable for the reason that these cells show no signs of degeneration; that they are found in the very heart of the tumor, and not alone in the periphery; and that they may be seen in all stages of differentiation.

There can be no doubt, therefore, that although the majority of the neoplastic cells are potential neuroglia cells, some are potential neurones, and it is on this basis that the designation of medulloblastoma has been adopted.

INVASION OF THE MENINGES BY MEDULLOBLASTOMAS

It has long been remarked that tumors of the fourth ventricle are prone to invade the meninges. There can be collected from the literature numerous cases of this invasion due to what we regard as undifferentiated medulloblastomas. The first was recorded by Ollivier (1837). Other reports have followed by Ross (1877), Schultze (1880), Turner

(1886), Richter (1886), Coupland and Pasteur, Case 2 (1887), Busch (1896), Nonne (1897), Weaver (1898), Michael (1902), Spiller and Hendrickson (1903), Rindfleisch (1904), Dercum (1906), Rosenblath (1906), Rach (1907), Martens and Seiffert (1908), Batten (1908-9), Wimmer and Hall (1913), Ford and Firor, Case 2 (1924). There are doubtless others. This list does not take into account the numerous cases of medulloblastomas or spongioblastomas of the cerebral hemispheres which have invaded the subarachnoid spaces, such as the cases of Westphal, Lenz, Löwenburg, Askanazy, Strauss and Globus, etc. We have had an example in our own series (which, in addition to the

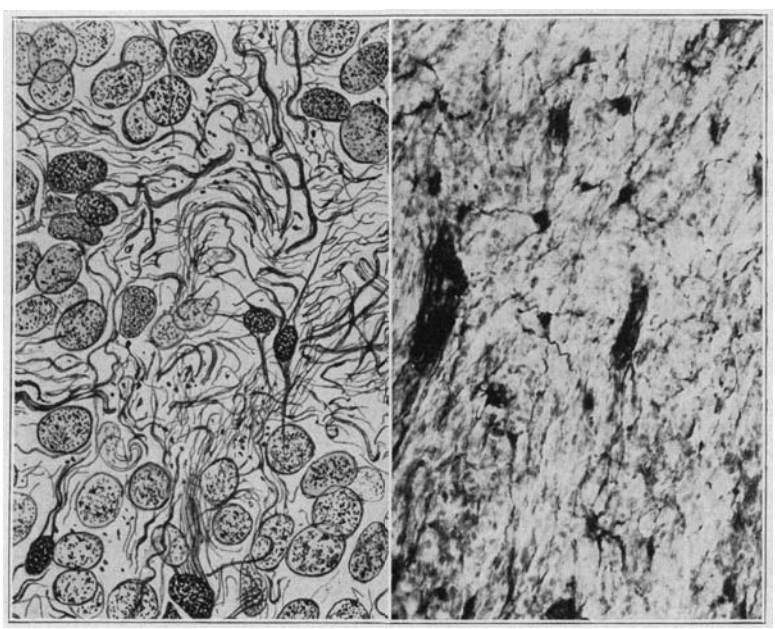

Fig. 31 (Case 19).—Result of differentiation on the nuclei of the cells. Hortega's fourth variant; ×850.

Fig. 32 (Case 22).—Astrocytes impregnated by Cajal's gold sublimate method; ×300.

twenty-nine examples of this report, comprises five cases of undifferentiated medulloblastomas of the cerebral hemispheres) of such a widespread extension. Numerous examples of primary medulloblastomas of the spinal cord which have invaded the meninges might also be added (Fischer, Grund, Schlesinger, Schlagenhaufer, etc.).

In our present series of twenty-nine cerebellar cases, the tumor in three of them had invaded the spinal meninges, while in the fourth (Case 5) it had spread widely over the cerebellar and cerebral hemispheres through the leptomeninges.

Most lesions of this kind have been described in the older literature under the term sarcoma or sarcomatosis, and more recently gliosarcoma, encephaloid sarcoma, etc. They are in reality composed of embryonic medullary cells, as has been remarked by many observers. We have definite reasons to believe that they are clearly distinguishable from the actual primary sarcoma of the brain, which is an exceedingly rare tumor and presumably must come from the walls of the blood vessls.

TREATMENT

The ultimate object of a study of this kind is the improvement of our therapeutic procedure for a given type of tumor. This can only come from increased knowledge of the exact situation, nature and manner of growth of the lesion. The table shows that attempts to extirpate these particular tumors totally are futile, and that even exposure and decompression may be accompanied by a high mortality. This is not a matter for surprise in view of the hazardous situation of the lesion which overlies the fourth ventricle and often projects for some distance down the spinal canal through the foramen magnum. That the operative mortality has not been greater may perhaps be taken as a matter for congratulation.

The temptation will always be present for the surgeon to attempt an enucleation in view of the apparent encapsulation of the tumor when approached from its posterior surface, but it is safe to say that a conservative attitude in this respect is the course of wisdom.

Our present feeling is that a simple suboccipital decompression followed by persistent roentgen-ray therapy offers the best results. The patients who survived the operation and were not given treatment with the roentgen-ray had an average survival of only seven months, while those treated by radiation, including only those who have died, have had an average survival period of more than nineteen months. Three of the patients are still alive. The tabulation of cases conveys of course no idea of the enormous subjective relief offered to these unfortunate children by the decompression during the postoperative survival period. The experience with the case last reported (Case 17) shows what may result and gives hopes for these desperate cases in the future.

SUMMARY

1. A series of twenty-nine centrally placed cerebellar tumors, arising from above the roof of the fourth ventricle and occurring mainly in children, has been described.

2. For these tumors the term medulloblastoma is proposed.

3. Evidence is submitted that they are composed mainly of indifferent cells, analogous to those described by Schaper in the developing cerebellum, and that most of these cells are potential neuroglia.

4. The surgical experiences indicate that the best method of treatment consists of a suboccipital decompression followed by persistent roentgen-ray therapy.

DISCUSSION

DR. HARVEY CUSHING: When Dr. Bailey and I began work on this particular group of tumors, we were unaware that they had previously been described as spongioblastomas. Indeed, it was not until we saw the program of the present meeting that we learned not only that Dr. Globus and Dr. Strauss were working on the same subject as ourselves, but also that they had already baptized the child. In view of their priority in this matter, we have most willingly acceded to the petition by Dr. Globus that his paper should be allowed to precede rather than to follow our own. This was as it should be. But, unfortunately, from what Dr. Globus has said and from the pictures he has shown, I fear we would not recognize our own child in anything but the name. It is futile, I think, to inflict on the Society any further discussion in this matter, and I propose that Dr. Globus and Dr. Strauss, Dr. Bailey and I foregather in some quiet antechamber and thrash this matter out together rather than to take the Society's time by doing so in open meeting.

Dr. Bailey has also prepared a diagram to indicate from what cells these tumors arise; and though it agrees in many points with the diagram Dr. Globus has presented, we favor the inclusion of two types of spongioblasts. From only one of these cell types do the tumors with which we are concerned take their origin, namely, from the very early spongioblasts or medulloblasts of the nervous system which antedate any differentiation into neuroglia. Dr. Globus and Dr. Strauss, I surmise, are dealing with a tumor much more akin to the true neuroglial tumor, for some of their slides show definite neuroglia fibers. All such tumors we have excluded from our group. We may possibly have leaned over backward in our effort to exclude all other tumors than those of one definite type, and our friends from New York may have leaned in the other direction in an effort to include as many tumors as they could within the grouping which they had made. Their tumors, moreover, appear to be cerebral in origin whereas ours with few exceptions have been found in the cerebellum.

Our tumors represent a type with which we have been familiar for a long time. As stated, they are tumors which usually give symptoms in the first decade of life, and they are often spoken of as tumors of the fourth ventricle. We are now so familiar with them that we could almost be certain of the diagnosis from gross appearances alone, without waiting for histologic verification. In addition to these twenty-nine there have been five with a similar histologic picture from other parts of the brain, but they are in some ways less distinctive than those of the midcerebellar type.

We are also familiar with the tumors which Dr. Globus has shown us. They represent a definite type of neoplasm, perhaps the most common of all gliomas, and include those which in former days were called gliosarcomas. Just what we may decide about them in the matter of terminology I cannot be sure; but at least either Drs. Globus and Strauss, or Dr. Bailey and I will have to recede from our proposed terminology and agree on some different term for these obviously different types of tumor.

Our midcerebellar gliomas are, I think, far less malignant lesions than those which Dr. Globus has presented, being more dangerous to life from their situation than from their malignancy. They, on the other hand, are more malignant than the ependymomas arising in this region — tumors of which Dr. Bailey has already made a detailed report.

It is for us neurosurgeons most important that we should know all that we possibly can regarding the different types of gliomas, which represent about 40 per cent. of all of our intracranial tumors. The prognosis of some of them is as favorable as that of any tumors of the nervous system; the prognosis in some extremely unfavorable. It is not until we can begin to regroup them, and this process carries with it the necessity of renaming them, that we can make any great advances. To make advances it is necessary that we, one and all, understand what the other man is talking about. The same name for two different conditions will hinder rather than help, and I trust that by the time of our next meeting Dr. Globus, Dr. Strauss, Dr. Bailey and I may have something further to say on the matter before the Society.[13]

Dr. Percival Bailey: I think the whole discussion hinges on the fact that we are calling two different things by the same name. Dr. Cushing and I make no claim to having invented the word "spongioblastoma" and are willing to give Dr. Globus credit for this excellent term.

The last lantern slide which we showed was copied from Castro's article on the evolution of the spongioblast. We are struck by the resemblance of the tumor cells to what Castro called the dislocated epithelial corpuscle.

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13. We at first decided to distinguish the two types by calling our tumors *spongioblastoma indifferentiale* and the tumor of Globus and Strauss *spongioblastoma multiforme;* but on more mature consideration it has seemed more appropriate to the tumors of the type we described to term them *medulloblastomas* and thus to avoid any further confusion. Hence the title of our paper has been changed.