

A CASE OF MULTIPLE EPENDYMOMATA OF THE BRAIN AND SPINAL CORD, WITH TABETIC SYMPTOMS¹

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Our object in presenting this communication is to direct attention to a diffuse tumor formation whose anatomical location was such as to excite gradual compression and destruction of the posterior nerve roots, resulting in a symptom complex closely simulating tabes dorsalis.

From a pathologic standpoint the case seems to stand alone, as we could find no record in the literature of a precisely similar case. Specimens were submitted to Doctors Mallory and Ordway, who entirely confirmed our view of the histologic character of the growth.

The patient, Mrs. R. W., married, entered the Samaritan Hospital December 17, 1909. Her age was fifty years and her occupation that of a housewife. Her chief complaint was that of recurring pains of a lancinating character, irregularly distributed in the lower limbs. The pains were very severe, of short duration, and were often followed by a numbness in the areas of the distribution of pain. In addition she complained of backache, double vision, and weakness in the limbs, and an unsteady gait.

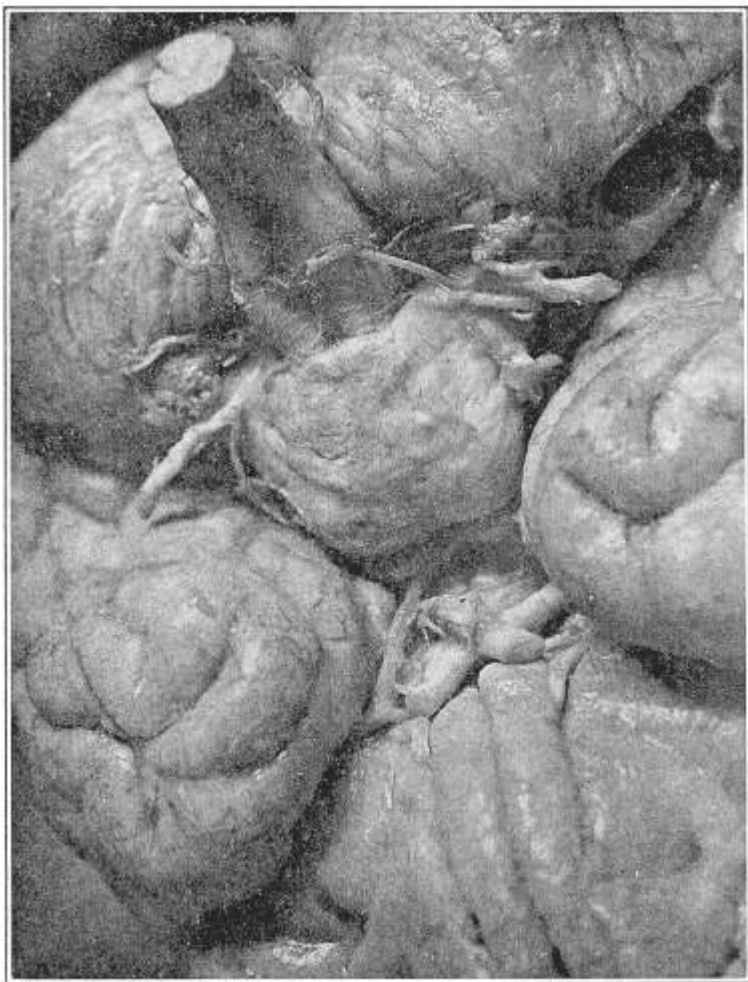
Family History.—Her father and mother are living, past ninety years of age, and are well. Two sisters and a brother died of tuberculosis of the lungs. One brother was killed accidentally. No history of nervous diseases or insanity in the family.

Personal History.—She has had the usual diseases of childhood. Menstruation was established at twelve years of age. She has always been regular and without pain. She married at the age of twenty-eight years, the result of which has been one healthy daughter. She has never had a miscarriage.

The present illness began two years ago, with lightning-like neuralgic pains in the lower limbs, which recurred frequently, with intervals, short or long, of perfect freedom from pain. On several occasions pain of a similar type occurred in the areas of distribution of the ulnar nerves. At first these attacks of pain

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occurred several times each day, but gradually the intervals were increased. About two months after the onset of the pains she developed a difficulty in locomotion, which she thought was due to a marked degree of unsteadiness. She stated that her gait had become so difficult of late that she had to give up going about at



Base of brain showing nodules on the pons and depression in the cerebellum.

night. These pains and the disordered condition of locomotion have progressively increased until at the present time she is just able to go about her rooms with the aid of two canes. She has some pain in the lumbar region on each side of the spine. She now complains of numbness in the feet and also in the ring and

little fingers of each hand. She has had no attacks of pain that at all resemble tabetic crises.

Physical Examination.—The patient is slenderly built, but fairly well nourished. Weighs 120 pounds, five feet two inches in height. There is no dyspnea, no edema or cyanosis, and no general emaciation.

Lungs.—The examination of the lungs shows nothing from the normal.

Heart and Arteries.—The heart dullness is normal. The apex is punctuate, and in the fifth intercostal space well within the left mammillary line. No adventitious sounds were discoverable. The systolic blood pressure was 140 mm. HG.

Liver.—Liver dullness is at the sixth rib in the right mammillary line and extends to the costal border; in the right axillary line it is at the seventh rib. The lower border of the liver is palpable and smooth. The spleen is not palpable or percussible. The right kidney is movable; the left is fixed.

The pelvic examination showed an anteflexed freely movable uterus, infantile in type. The lymphatic glands were not palpable. No evidence existed whatsoever of a past luetic infection. The urine showed a specific gravity of 1020. It was acid in reaction; clear amber; contained no sugar, albumin or casts. It contained epithelium, urates and uric acid crystals.

NERVOUS SYSTEM

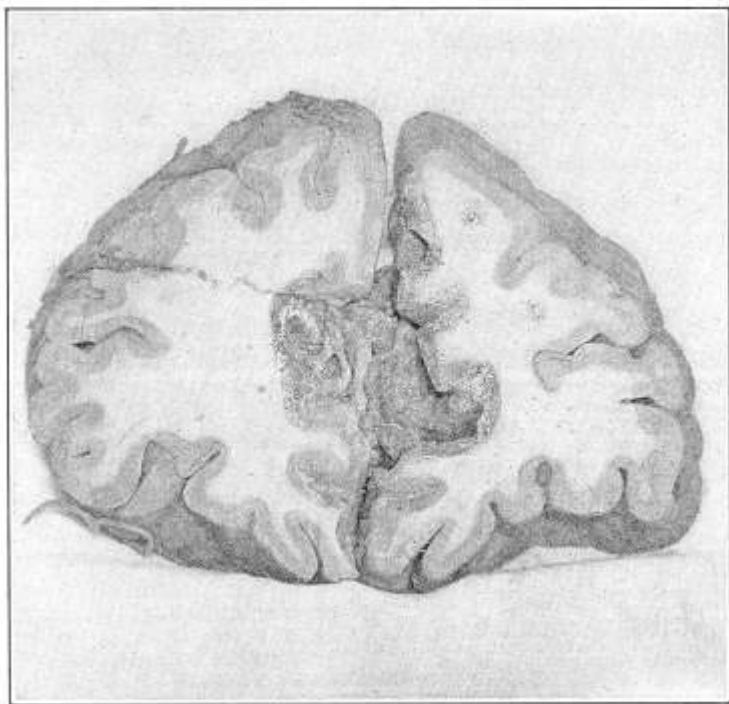
Cranial Nerves.—The pupils are equal, spheric, small. Respond to light and accommodation and consensually. They react on each side to irritation of the cervical sympathetic. All movements of the eyeballs are normally performed save the outward rotation of the left eyeball, due to paralysis of the left external rectus muscle. There is a moderate degree of ptosis on each side. There is no reduction of the visual fields, no exophthalmos and no nystagmus. The ophthalmoscope shows no changes in the discs or retinæ. The facial muscles are symmetric and functionate normally. The tongue protrudes in the median line, and presents no tremor or atrophy. There is no difficulty in deglutition. The hearing is perfectly normal on each side, and both smell and taste are intact.

Gait.—The gait is typically ataxic. The patient throws the feet well forward and outward, and they come down to the ground on the heels with a stamp. When the patient is asked to walk a seam or chalk line she exhibits the most extreme incoördination, whether she proceeds forward or backward. Rombergism is very marked. The finger nose test brings out marked ataxia in the upper extremities. There is marked hypotonia in the lower limbs.

Sensation.—Several small areas of anesthesia were found existing between the knees and ankles, particularly about the ankles and just above them. There is distinct retardation to the conduction of painful impressions in each lower limb. The muscular

sense is very much reduced. The muscles show no wasting, and the electrical reactions are perfectly normal. The muscular strength seems perfectly normal, and no apparent weakness exists.

Reflexes.—Both patellar tendon and tendo Achillis jerks are absent. The plantar reflexes are feebly present. The wrist and triceps tendon reflexes are absent. The infra-umbilical reflex on each side is absent, but the supra-umbilical reflex is present. The organic reflexes are perfectly controlled.



Area of softening in the frontal lobes. Actual size.

Mental State.—Her memory is defective and her cerebation slow. She can, however, read and write perfectly, and shows no evidences of aphasia. She has never had local or general convulsive seizures.

Twelve c.c. of a clear crystal-like fluid were removed by lumbar puncture on December 24, 1909. Centrifugalization brought down no sediment. No cells were found and no growth on blood serum occurred. A diagnosis was made by the pathologist of a transudate from the spinal canal. Unfortunately neither a Wassermann nor Noguchi reaction was made. There was no tenderness,

deformity or rigidity of the spine. She showed while in the hospital no evidences of improvement. Her mental symptoms became progressively worse, her memory much more defective, her cerebration very slow. She became drowsy, lost control over her organic reflexes, and finally passed into a stuporous condition and died in coma.

AUTOPSY 199, RECORDS OF THE CLUETT PATHOLOGICAL LABORATORY, SAMARITAN HOSPITAL

Mrs. R. W., æt. 50. Died Jan. 6, 1910, 5 P.M. Autopsy Jan. 7, 1910, 9:30 A.M.

Body of an emaciated woman 150 cm. in length. Rigor mortis present. Moderate edema of feet and ankles. Emaciation greater in upper than in lower extremities. No glandular enlargements. Post mortem lividity well marked. Bedsore moderate in extent over right buttock.

Abdomen.—Panniculus adiposus moderately decreased in amount. There is no fluid in the peritoneal cavity. The peritoneal surfaces are smooth and glistening and show no adhesions. The diaphragm extends to the fifth rib on the right and to the sixth space on the left.

Pericardial Sac.—Contains a large amount of clear fluid of a yellow color. The surfaces are clear. The fat is normal in amount.

Heart.—The right ventricle contains a few chicken fat clots but is otherwise clear. The right auricle is clear. The mitral valve is somewhat thickened but competent. The mitral orifice is slightly contracted, measuring 4.5 cm. in circumference. The anterior cusp is intimately blended with the posterior so as to form one leaflet. The aortic valves are normal. The muscle is of good color and consistency. The aorta shows a few slight patches of sclerosis about the base.

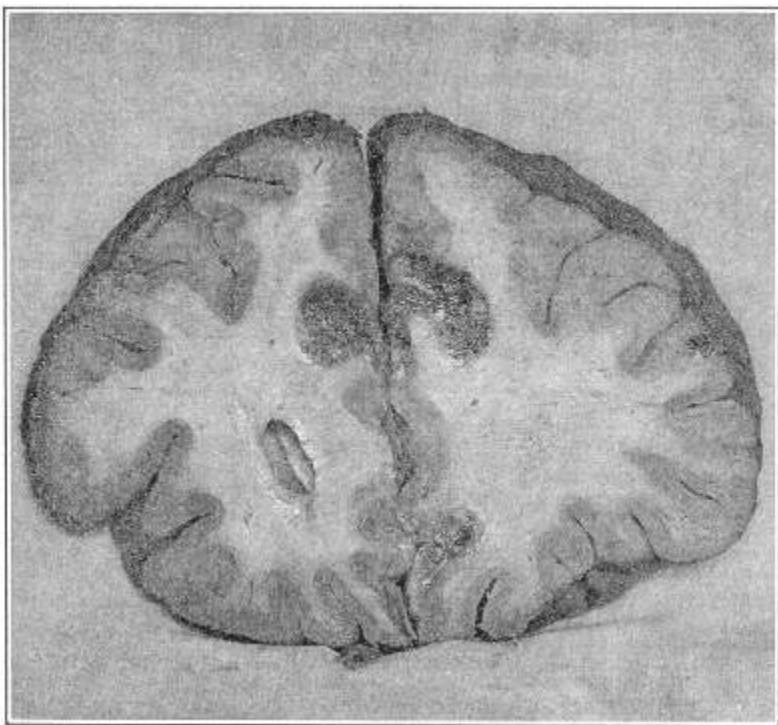
Pleurae.—The left shows a surface slightly mottled with lighter areas than the rest of the surface. It is smooth and glistening save for a few fibroid adhesions at the apex. The right pleura is clear.

Lungs.—The left shows slight mottling over the surface and the lighter areas are firmer in consistence than the remainder. On section these areas are seen to be solid, do not crepitate and project above the surrounding tissue. The whole lower lobe is studded with these nodules, which vary from 0.5 to 5 cm. in diameter. The upper lobe is air-containing and apparently normal except an old fibrous scar at the apex.

The right lung is air-containing throughout, is smooth and mottled slightly with coal pigment on the surface. On section the cut surface exudes copious amounts of blood-tinged fluid. The color is deep red. The bronchi show nothing noteworthy. There is a fibrous scar at the apex similar to that in the left.

Spleen.—Is very small, measuring 5 by 5.5 by 3 cm. The consistence is firm. The Malpighian bodies are not prominent. The trabeculae are slightly increased in amount at the expense of the pulp.

Kidneys.—Both are alike. The capsule peels readily, leaving a smooth surface. The cortex is firm and 6 mm. in depth on the average. The pyramids are slightly congested. Otherwise nothing abnormal is noted.



Area of softening in the frontal lobes. Actual size.

Adrenals.—No changes are noted.

Pancreas.—Negative.

Stomach and Intestines.—Negative.

Appendix.—In the right iliac fossa and seems slightly atrophic.

Bladder and Genitalia.—Negative.

Brain.—The dura shows no thrombosis of the sinuses and the general contour is fairly normal. The pia does not appear thickened. There is some congestion of the blood vessels. On the right hemisphere between the termination of the fissure of Ro-

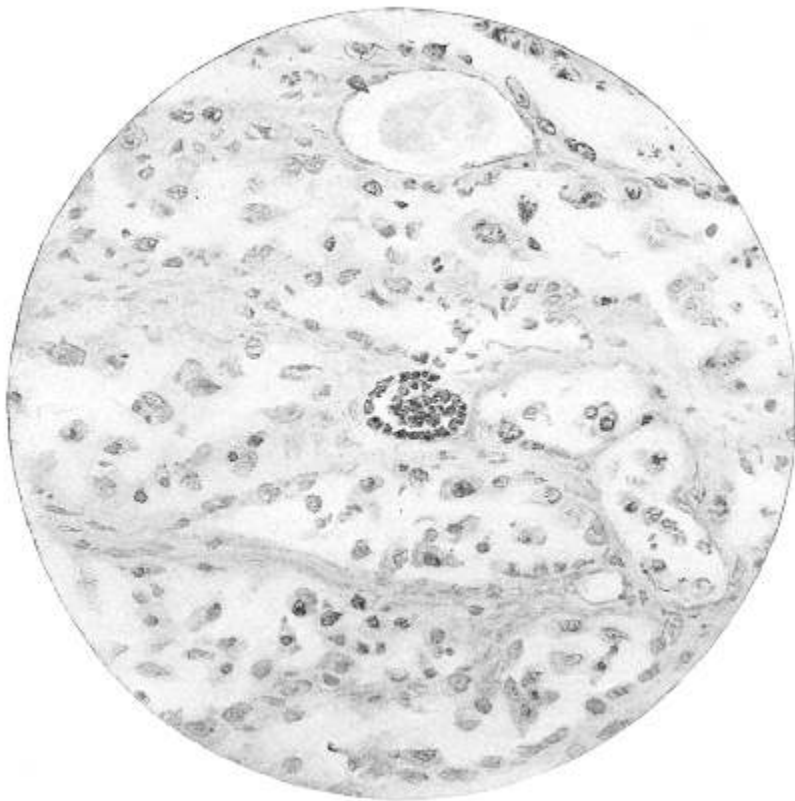
lando and the median fissure is a depressed portion of cortical tissue 2 cm. in diameter and 1 cm. in depth. On the opposite hemisphere 2 cm. from the fissure of Rolando and at the junction of the frontal and parietal lobes is another depression 1 by 1.5 cm. Another 1 cm. deep and about 1 cm. in diameter is seen on the anterior surface of the right lobe of the cerebellum. All these depressions are bridged over by a delicate fold of pia stretched tightly across the top. The pons is somewhat whiter than usual. Over its surface are numerous small nodules and sharp projections from 1 to 3 mm. in size. They are not at all prominent and do not deform the surface to any extent, nor do they look like tumor masses.

The cord is removed in toto and shows no abnormality to the naked eye. The brain and cord are hardened in formalin to be sectioned later.

Brain after Hardening.—Transverse sections are made through the brain about 1 cm. apart. The sections through the cerebellum, occipital, temporal, parietal and central gyri showed no macroscopic changes. The ventricles are all somewhat dilated, but, owing to the process of hardening, the existence of fluid in excess cannot be determined. The lateral ventricles show the most dilatation, and with good reason. They are filled with what appears to be a grayish white, soft, edematous-looking mass of tissue. On closer examination this tissue seems cellular in nature and to be attached to the walls of the ventricles by a fibrous membrane. In some places, owing doubtless to the shrinking power of the formalin, it is separated from the walls, but for the most part it is quite firmly adherent to them. Sections through the depressions in the cortex show no abnormality other than the deformity. The gray matter follows the outline of the depressions and the subjacent white matter seems only a trifle compressed thereby. There is apparently some thinning out of the gray matter, however. The same is true for the depression in the cerebellum. It almost seems rather to be a widening of the sulci at these points than any degeneration or tissue destruction. All the tissue in this region is normally firm in consistence.

In the section just ventral to the precentral sulcus one sees in the gray matter of the frontal lobe, 1 cm. from the median surface, a small round area of softening about 5 mm. in diameter. It is grayish in color, soft in consistence and dotted with small punctuate hemorrhages. In the section 1 cm. forward of this there appears another area of softening in the right hemisphere in the same relative position and of the same size and general appearance. At the same time the original area in the left hemisphere has doubled in size, become softer and approached the median surface. As the sections progress forward these areas gradually enlarge to a maximum of about 5 by 6 cm. over the median surface and 1 cm. deep. They involve the surface on

both sides of the fissure, and each becomes smaller as the sections advance until each vanishes at about 5 mm. from the anterior pole of the frontal lobe. These areas of softening present a ragged, worm-eaten appearance and involve the gray matter only. In color they are reddish gray in the deeper portions where there is apparently some degeneration and softening of the cortex, but on the surface the grayish white color noted in the mass in the



Growth in ventricle (lateral) Eosin-methylene blue stain. $\times 400$.

ventricles predominates. They are surrounded by punctuate hemorrhages in the white matter. These areas, where there is not too much of the surface destroyed, follow the general contours of the convolutions, though the growth is much more irregular and rugose than the normal brain.

Sections of the pons show the nodules more distinctly than the mere surface view. They do not dip down into or invade the pontine substance but rather project above it as small yellowish

or ivory colored nodules firm to the touch and which appear almost as if continuous with the pia. This latter point is impossible to determine, however.

On section the cord shows nothing abnormal grossly.

Anatomic Diagnosis.—Areas of softening on the median surfaces of both frontal lobes of the cerebrum. Chronic mitral endocarditis. Broncho-pneumonia of left lung, lower lobe. Edema of right lung.

Microscopic Description. *Heart.*—The endocardium is slightly thickened. There is a trifling increase in the interstitial connective tissue here and there. Otherwise the heart is normal.

Lung.—Areas of intense polynuclear infiltration completely fill some of the alveoli lying in clusters about the ends of the finer bronchi. The latter also show some polynuclear infiltration, together with desquamation and degeneration of the epithelium. The alveolar and bronchial walls show great vascular congestion and anthracotic pigmentation. Between these areas of infiltration the alveoli are empty, and the majority are ruptured into one another and are extremely thin-walled.

Liver.—The lobular arrangement of the gland is marked, owing to a most marked infiltration of the liver cells in the lobular centers by fat droplets, leaving only a thin shell of normal cells at the peripheries of the lobules. The capillaries are quite generally engorged with red cells. There is a very slight increase of connective tissue about the portal spaces associated with an infiltration of round cells.

Spleen.—The capsule and trabeculae are thickened. There is slight increase in size of the Malpighian bodies. The central arteries show some hyaline degeneration. The pulp is congested and contains some free hematogenous pigment.

Kidneys.—The capsule is not thickened. Some excess of connective tissue is noted in the cortex. The epithelium of the convoluted tubules is swollen and granular. The large vessels are everywhere congested.

Adrenals.—Normal.

Intestines.—The superficial mucosa shows slight degeneration and some necrosis, with many desquamated cells and congested blood vessels. There is some round cell infiltration in the sub-mucosa.

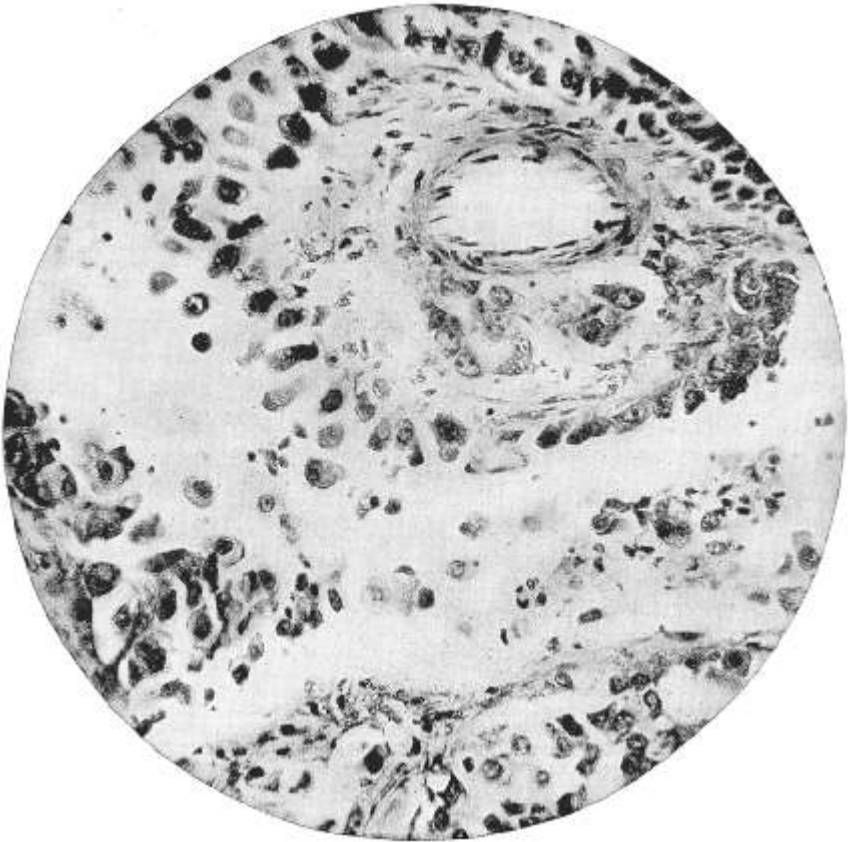
Stomach.—A similar condition to that in the intestines is here shown, but a little more marked.

Bladder.—Normal.

Pancreas.—Normal.

Brain.—The sections herein described were stained with the following: hematoxylin and eosin, eosin-methylene blue, phosphotungstic acid, hematoxylin, Mallory's connective tissue (aniline blue) stain, Weigert's, van Gieson's and safranin. Celloidin and paraffin embedding were used.

The section from the wall of the lateral ventricles, and including the growth found therein, show that the ventricles are filled with a cellular tissue closely attached to the walls. This mass is made up of cells generally alike in the essentials but differing slightly in minor details. In their arrangement they seem in all cases to be placed in single rows about irregular spaces not unlike



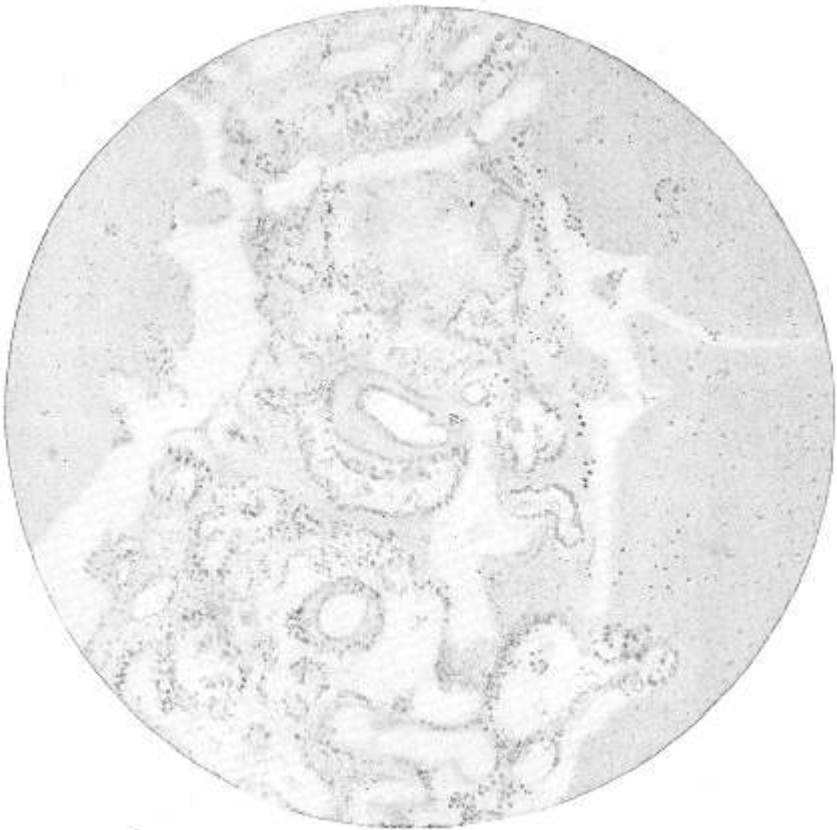
Detail of growth in lateral ventricle. Eosin-methylene blue stain. $\times 600$.

a glandular formation, the whole, therefore, roughly resembling an adenoma in structure. The cells are, for the most part, irregularly columnar, though some are polygonal or cuboidal. The nuclei are nearly all vesicular and are large and irregularly rounded or oval. The chromatin network is especially marked in the eosin-methylene blue stains. A nucleolus is nearly always present in each nucleus, the exception being in those pycnotic

nuclei which are visible here and there throughout the entire section. These pycnotic nuclei take a much deeper, more homogeneous stain, show no chromatin network whatever, and are small and shrunken looking. Many of the cells are doubly nucleated, and one or both of the nuclei shows pycnosis. Indeed, the majority of the nuclei that are pycnotic are in these doubly nucleated cells. The supporting framework upon which these cells rest is made up of very fine strands of connective tissue of the white fibrous variety running in a coarse network throughout the growth. The protoplasm of the cells takes varying grades of eosin stain from eosin to bright carmine. In general those showing the most degeneration of the protoplasm take the most brilliant eosin stain. The protoplasm is finely granular or cloudy. None of the cells shows vacuolization, not even the most degenerated. Nor is there any coarse granulation or hyaline degeneration. The degenerative process seems to produce a fine granular fragmentation of the protoplasm while the nucleus disappears by karyorrhexis or karyolysis, examples of both being found in a single field. The cells from a whole alveolus here and there are desquamated and lie in the lumen in a single degenerated mass. It is a curious thing that in none of these single alveoli is there any other nuclear destruction than karyolysis, no nuclear dust or coarser fragments being found. The degeneration is not confined to single alveoli, however, for areas are seen comprising many alveoli together in which the cells have degenerated and become necrotic en masse. The cells are represented by a fine dust-like detritus completely amorphous or more or less conformed to the original cell outlines. In many of these areas the supporting framework of connective tissue has shared in the general destruction and the alveolar structure is lost. The growth as a whole shows no invasive tendency, its confines being sharply limited by the walls of the ventricles. There is, however, no encapsulation. Such connective tissue as is present is in the form of the supporting framework. In this connection it may be noted that neither here nor in any of the other portions involved by the growth are there more than the fewest possible number of mitotic figures. Safranin stained sections show possibly one mitosis to twenty fields. The few figures that are found present fairly regular division with clear cut dyasters, spindles and skeins. The normal ependymal lining of the ventricles is nowhere to be seen. The growth is applied directly to the bare ventricular walls except in some places where the shrivelling power of the formalin had apparently torn it away. The surrounding brain tissue shows no changes whatever.

In the sections taken from the softened areas on the median surfaces of the frontal lobes the same general structure of the growth obtains. Here the necrosis is, however, far wider and more complete. The surrounding brain tissue too has been

greatly involved, in striking contrast to the immunity of the periventricular tissue from the necrosis in the growth there seen. The subjacent cortical matter is apparently involved by direct continuity from the superficial necrosis in the growth rather than by any invasion of the tumor mass into the brain substance and consequent destruction. Nowhere in areas not degenerated can any such invasion be found. The cell growth which at the mar-



Growth on frontal lobe. Eosin-methylene blue stain. $\times 100$.

gins of the necrotic area is about 2 mm. thick narrows down gradually as it spreads away from the necrotic patch until it finally becomes a single row of low columnar and cuboidal cells, the nuclei of which take a denser, more homogeneous stain than the rest of the mass shows. The protoplasm here is also darker and more cloudy. This line of cells at last ends abruptly and gives place to the normal pial structure on the surface which beneath

the tumor mass had been obscured. Here and there over the cortex a single layer of cells corresponding precisely to these makes its appearance, three or four cells being grouped together or a longer chain extending over an entire convolution being found. The necrosis in the brain tissue beneath the cell mass is extensive. Sometimes it involves the whole cortical substance quite down to the white matter. The latter is nowhere touched, however. A most peculiar thing is that while the necrosis of the gray matter is so extensive the substance immediately surrounding is nearly if not quite normal. The transition from total necrosis to normal tissue is strikingly sudden. The only changes that are visible in the adjacent substance are numerous small capillary hemorrhages scattered here and there and some engorgement of the smaller blood vessels. The latter are often the seat of a slight round cell infiltration.

Sections through the pons reveal the fact that the small nodules which were seen upon its surface are composed of little aggregations of cells identical in morphology and general arrangement with those already described. These tiny masses of the tumor cells have at most two or three of the small alveoli before described and they taper off into single rows on either side of the nodules exactly as did the cells on the median surfaces of the frontal region. Sections from the medulla show only a few of these nodules, but they correspond to those on the pons.

On examining the sections from the cord at varying levels a much different and most interesting condition is found. Beginning at the level of the second cervical vertebra and continuing the whole length to its breaking up into the cauda equina we find that the tumor mass is again in evidence. It forms a continuous structure this entire distance. In its arrangement it is a replica of the growth elsewhere described. It is gathered into small rows or strands surrounding empty spaces and has the same supporting framework of fibrous tissue. The cells are the same in their general characteristics save that here there are fewer in the mass of the tumor showing pycnotic changes. Safranin stains reveal a slight increase in the number of mitotic figures, but even here there are very few. Again we find not the slightest tendency to any invasion of the tissue of the cord or nerves. There are no areas of necrosis to be seen throughout its entire length. The remarkable point about this portion of the growth is that it is confined practically wholly to the posterior surface of the cord. It extends only approximately half way around and ends abruptly in a short row of single cells. The bulk of the growth showing the pronounced alveolar structure is heaped up about the posterior nerve roots and completely encircles them. Here it shows a somewhat more compact arrangement. The alveolar spaces are smaller and the fibrous tissue framework is heavier, denser and larger in amount. This is so apparent that it has seemed definitely

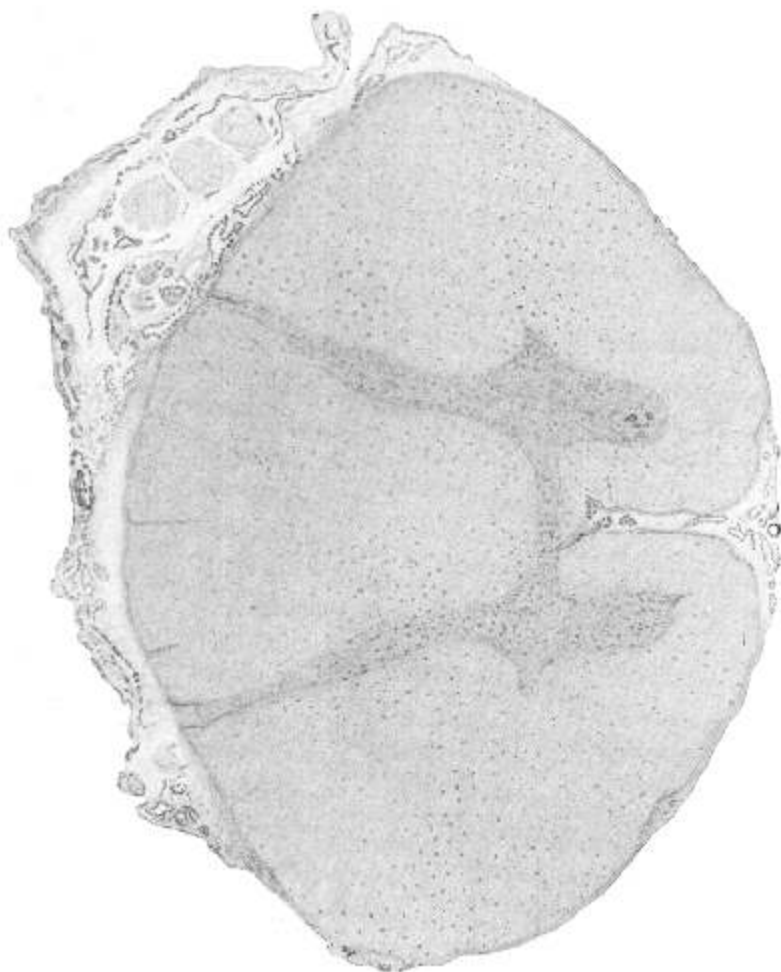
to have compressed the posterior roots, for they are smaller than normal and embedded in a dense mass of fibrous tissue and tumor cells. The heaping up of the tumor is most noticeable about the nerve roots and is much thinner over the surface of the posterior columns intervening. There is very little to be made out as to the condition of the cord itself in the ordinary stains, but the Weigert sections give us a most interesting picture. Here one finds first of all the most strikingly brought out that there is great



Section showing degeneration of the entering posterior nerve roots.
Weigert stain. $\times 100$. Tenth dorsal segment.

degeneration of the posterior roots in the dorsal region especially. The myelin sheaths stain very poorly or not at all. There are a few fibers that seem to be intact, but the majority show total loss of the myelin substance or a gathering of this substance into small globules along the course of the nerve sheath where a longitudinal fiber is shown in section. The fibers as they enter the cord are greatly degenerated even down into the depths of the cord sub-

stance. In the posterior columns one also sees a widespread degeneration, though not nearly so complete as that in the nerve roots. The degeneration is somewhat irregular in its intensity. Patches here and there are almost totally destroyed and these



Lower dorsal cord. Showing distribution of tumor mass. Eosin methylene blue. $\times 20$.

gradually merge into and are separated by areas where there are relatively far more normal fibers. The greater part of the destruction seems to be in the posterior and central portions of these columns. The portions bordering on the posterior horns and the commissure are practically devoid of fibers showing degeneration. The rest of the cord, white and gray matter alike, is untouched.

The intensity of the degeneration seen in the posterior roots and columns is roughly in direct ratio to the amount of the tumor growth on the posterior surface. Both are most pronounced and heaviest in the dorsal regions, less so in the lumbar, and least of all in the cervical and upper dorsal. There are a few scattered cells of the tumor mass over the anterior surface and nestling in the anterior fissure, but they are very few indeed. There is no degeneration of the anterior roots or cords to correspond and, indeed, the tumor cells in that region are completely insufficient to cause any such change.



Lower dorsal cord. Showing degeneration of posterior roots and columns. Weigert stain. $\times 20$.

Revised Diagnosis.—Slight chronic mitral and mural endocarditis. Slight chronic interstitial myocarditis. Broncho-pneumonia of lower lobe of left lung. Edema of right lung. Fatty degeneration of the liver. Chronic interstitial splenitis. Acute catarrhal enteritis and gastritis. Multiple ependymomata of the ventricles, pons, cerebral cortex, medulla and posterior portion of the cord producing degeneration of the posterior spinal nerve roots and posterior columns by compression.

The pathologic findings may be summarized as follows:

I. A diffuse new growth derived from and having its primary location in the ependymal lining of the ventricular spaces of the brain.

II. A widespread involvement of the frontal lobes, with marked necrosis of the growth proper and the surrounding brain tissue.

III. Multiple nodules of the crura and pons, implicating the sixth nerve roots of the left side especially.

IV. Implication of the posterior nerve roots and dorsal aspect of the spinal cord throughout its whole length.

It seems to us that the location of the pathologic changes found in this case explains beautifully the symptoms from which the patient suffered during the last two years of her life. The sudden attacks of recurring pains, the incoördination and ataxia, the Rombergism, the loss of the patella and tendo Achilles jerks, the characteristic gait, loss of muscle sense, the retardation of the conduction of pain sense and the anesthetic areas, were doubtless due to the anatomical limitation of the diffuse ependymal growth to the dorsal aspect of the whole length of the spinal cord, implicating especially the dorsal spinal nerve roots which are absolutely encircled as if encuirass by the cellular proliferation, causing compression and atrophy of them, together with secondary ascending degeneration of the dorsal columns.

The paralysis of the left external rectus muscle was occasioned by degeneration of the left sixth nerve.

The mental symptoms, consisting of progressive loss of memory, slow cerebration and general mental enfeeblement (frontal lobe symptoms), were due to the widespread areas of necrosis resulting from the ependymal growths which involved the frontal lobes.