DIFFUSE SARCOMA OF THE CEREBRAL AND SPINAL PIA MATER.

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Tumors of the soft membranes of the brain and spinal cord, especially those of a diffuse character, are comparatively rare, and a careful study of each individual example is of distinct value. The following case was kindly offered me for study by Prof. Ludvig Hektoen, to whom I am indebted for much assistance in the preparation of my report.

Primary tumor of cerebrum, secondary diffuse sarcoma of the cerebral and spinal pia mater.—W. C., male, aged 11 years, entered the Presbyterian Hospital December 31, 1896, in the service of Dr. A. C. Cotton. Clinical diagnosis, tubercular meningitis.

Family history negative. No tubercular or specific history obtainable. Present illness began September, 1896, with convulsions, in which the whole body was rigid and the eyes fixed. Before the convulsions the patient was dizzy and vomited; after them he would sleep for a time, and upon waking would be delirious. At times he was confined to bed.

Examination on admission: Confined to bed, poorly nourished, skin warm and moist, countenance staring and flushed at times, pulse regular and rapid, Cheyne-Stokes respiration, bowels constipated, pain in head and neck; only partly conscious, moves but little, but there is no paralysis; eyes bulging, pupils widely dilated, sight much impaired, the right eye insensible to light, the left to sensation; nystagmus marked, double optic neuritis; temperature 98.8° F., pulse 100. Hyperæsthesia over entire body. Pain on percussion over the cranium. *Taches cérébrales*. From this period until death there were recurring convulsive paroxysms, sometimes several in a day, and again only at intervals of several days. There were, later, delirium and involuntary evacuations. Death took place April 13, 1897.

Autopsy by Dr. Hektoen.—Body small and extremely emaciated; head large; thyroid gland large. Larynx and trachea normal. Pleuræ smooth

and empty. Over the anterior surface of the right lower lobe is a circumscribed area in which the pleura contains numerous grayish-yellow, pin-head and larger, disc-like nodules. The peribronchial lymphatic glands contain tubercular areas. Lungs normal save for circumscribed areas of grayish-red consolidation in the lower lobes. Heart small; endo- and myocardium normal; pericardium smooth. Aorta normal. Spleen, kidneys, pancreas, liver, stomach, intestine and adrenals normal. Mucous membrane of urinary bladder red, rough and covered with shreddy material.

Upon opening the cranial cavity a large amount of very slightly turbid fluid runs out. Dura mater normal. The pia mater upon the optic commissure, the medulla and the upper part of the spinal cord is the seat of a reddish, indistinctly nodular thickening. Around the apex of the left frontal lobe is a similar area. The entire posterior surface of the spinal cord is the seat of marked thickening, so that the pia is reddish and somewhat lobulated, and the volume of the cord appears to be greater than normal. It fills the dura, and when the latter is cut masses are forced out through the opening. The ventricles of the brain are greatly dilated, containing a clear fluid.

Anatomical diagnosis.—Sarcoma of pia mater of brain and spinal cord. Hydrocephalus. Broncho-pneumonia. Acute cystitis. Chronic tuberculosis of the peribronchial lymph glands and pleuræ.

Description of the brain.—There are irregular areas of a gelatinous, opaque, whitish-gray substance in the pia mater, scattered over the anterior surface of the medulla and the pons and spreading out over the lower surface of the lobes of the cerebellum. The largest area upon the cerebellum is on the right lateral hemisphere, being 4.5 cm. from before backward and 2 cm. wide at the thickest part. This lies parallel to the fissure between the lateral and median lobes, extending outward from the fissure. This area is not elevated above the surface but appears to involve the underlying substance. From this area a thinner growth extends continuously over the lower surface of the median lobe, becoming less dense as it approaches the left lobe. Upon the left lobe, lying in a position symmetrical to that on the right, is an area of growth 1.5 cm. antero-posteriorly and 0.75 cm. transversely. This is slightly elevated above the surface and somewhat firmer than the corresponding area on the opposite side. Scattered over the under surface of both lateral cerebellar lobes and along the front of the medulla and pons are areas of growth varying in size from those which are very minute to those 0.5 cm. in diameter. The largest of these are elevated above the

surface and are firmer than the larger areas upon the cerebellum. They appear to bear no relation to the vessels in their distribution. On the upper surface of the optic commissure and optic nerves at their origin are globular masses of growth 0.5 cm. in diameter, which are partly continuous, thus forming an irregular, uninterrupted mass along the optic commissure and nerves. The apex of the left cerebral hemisphere is soft and somewhat collapsed. The surface for about 3.5 cm. from the apex, on all sides except below, presents the same sort of growth as that found on the cerebellum. It is, however, of a more pinkish-gray color. The tissue underlying this surface growth is very soft. A few small discrete masses of growth are seen at short distances from the larger area over the surface of the left cerebral hemisphere.

The brain was hardened in Müller's fluid containing 5 per cent of formalin. On cutting the left cerebral hemisphere into vertical sections, each 2 cm. thick, it is found that the centrum ovale of the left apex is replaced by a tumor extending antero-posteriorly 5 cm.; its diameter at a depth of 2 cm. is 5 cm., and at a depth of 4 cm. is 4 cm. The growth is extremely soft, and of a pinkish-gray color. In the sections the tumor mass tends to fall away from the surrounding tissue. The lateral ventricle is empty, very much dilated, its wall smooth, and the choroid plexus unaltered. Corresponding sections of the right hemisphere show the lateral ventricle to be similar to the left. This hemisphere is otherwise normal.

The fourth ventricle is filled to distension with a reddish and in parts grayish tumor mass. This is very soft, contains much blood and is continuous with the walls of the ventricle. It measures antero-posteriorly 4.5 cm., transversely 3.5 cm., and vertically 2.5 cm.

The spinal cord.—The cord, which was hardened in 5 per cent formalin, appears very much enlarged in the dorsal and lumbar regions. In the lower dorsal region it measures 1.75 cm. antero-posteriorly and 2.5 cm. transversely. The growth externally is slightly nodular and uneven, opaque and whitish-gray. In the upper dorsal region the blood-vessels are large and prominent. The growth extends over and between the nerves of the cauda equina. On section the cord itself is found to be of about normal size, the apparent enlargement being due to a growth of new tissue about it. The tumor growth is most abundant posteriorly, and is thickest in the lower dorsal and lumbar regions, where it is 0.75 cm. in thickness; it becomes much thinner in the cervical and upper dorsal regions. The growth in front of the cord also extends throughout the entire length, being more largely developed in the lower dorsal

and lumbar regions. It is nowhere more than 1 or 2 mm. thick. Laterally the growth is more abundant in the lower portion of the cord, where it is from 2 to 3 mm. thick and completely surrounds the posterior roots and to a less extent the anterior roots of the spinal nerves. The posterior roots appear very large from the tumor deposit. In the upper part of the cord the lateral growth exists as a very delicate, thin layer.

MICROSCOPIC EXAMINATION.

Spinal cord.—Weigert's stain. The cord is usually normal except in some places along the posterior border, where it is invaded for a short distance by the tumor.

Hæmatoxylin and eosin. The tumor is usually sharply limited at the border of the cord by a fibrous structure consisting of the altered pia mater. There is a growth of tumor tissue along the normal trabeculæ which pass from the pia mater into the cord. Posteriorly the cord is directly invaded by the tumor for a short distance. The tumor is everywhere of the same structure, consisting of closely-packed, small, round cells, with deeply-staining nuclei. The intercellular structure is usually but little developed, and in most places appears as a homogeneous material, staining faintly with eosin. Where the cells are not so closely packed it is finely fibrillated. In some places the connective tissue framework is more largely developed, appearing as quite heavy bands, but with little tendency to any regularity of arrangement. The blood-vessels are large and numerous with well-developed walls. In the cervical and upper dorsal regions the tumor is less than in the lower parts, but exists upon all sides. It is here thinnest at the sides and most marked posteriorly. The nerve-roots are here more or less surrounded by the growth, which has not penetrated the nerves themselves. In the lower dorsal and lumbar regions the growth is also least laterally and most developed posteriorly. The posterior nerve-roots, and to a less degree the anterior roots, exhibit an infiltration of the epineurium and perineurium, but the endoneurium has not been invaded by the tumor. Some of the larger vessels and bands of fibrous tissue have undergone hyaline degeneration. In the cauda equina the growth surrounds the nerves, but only in a few places was the endoneurium penetrated by tumor cells.

Brain.—The tumor in the apex of the frontal lobe consists of small round cells with deeply-staining nuclei, like those in the spinal growth. The arrangement of the vessels and the trabeculæ of the fibrous framework produces a somewhat alveolar appearance in places. The growth in the cerebral pia mater is similar to that in the spinal.

Sections were made of the tumor growth in the fourth ventricle, including the adjacent cerebellar tissue with its covering of pia mater, which appeared very slightly thickened. There is everywhere a thin layer of new growth following the pia mater over the convolutions of the cerebellum. The cells penetrate to a very slight extent the brain substance. The blood-vessels are very numerous, many being of large size. There are large and small areas of hæmorrhage into the tumor, some being quite recent with well-preserved blood corpuscles; others old, with remnants of blood-cells, fibrin and blood pigment.

Lungs.—In the lungs, on and near the pleura, are small areas of tubercular infiltration, containing foci of caseation, giant cells and tubercle bacilli. In the lungs are some areas of cell accumulation which resemble those in the tumor of the brain and cord. In these no caseation or giant cells are seen. From the histology of these areas it is impossible to decide whether they are metastatic tumors or not.

I have collected from the literature ten reports of diffuse meningeal sarcoma, of which the following are abstracts:

I. (Coupland and Pasteur.*) Female, aged 22 years. Course of illness about 4 months. Began with headache and morning sickness; later there were pains in the right shoulder and arm. A month before death pain along the spine; two days before death constant occipital pain radiating to the right shoulder and arm, double optic neuritis, paralysis of both external recti, tenderness of scalp, hyperæsthesia along the spine, weakening but not paralysis of the legs, and absence of knee-jerk; sphincters acted normally; no convulsions.

Autopsy.—Soft, jelly-like masses of new growth scattered over the meninges beneath the dura in the posterior fossa, about the body of the sphenoid and backward almost continuously to the foramen magnum. Medulla and pons uniformly invested with similar growth in which both sixth nerves were completely embedded. Spinal cord uniformly ensheathed in a semi-translucent, softish growth of a grayish-white color, the tumor being most developed on the posterior and lateral aspects of cord. Nerves of cauda equina surrounded by thin sheaths of new growth, which at intervals expanded into small tumors. The cord itself normal in shape and appearance throughout. The new growth was a small round-celled sarcoma, which followed the trabecular ingrowths of the pia into the cord. Brain normal.

* *Trans. Path. Soc.*, London, xxxviii (1887), 26.

II. (Coupland and Pasteur.*) Female, aged $4\frac{1}{2}$ years. Duration of illness about 3 months. Following a fall the child became irritable, developed a squint, and at the end of a month was unable to walk. Pain in upper part of back and head was followed by sudden blindness six weeks from the onset. Two months from the beginning was conscious and intelligent; pupils dilated and insensitive, blindness, pain in back and head. Optic discs gray and indistinct. General muscular weakness without atrophy, normal tactile sense, *taches cérébrales*. No convulsions.

Autopsy.—A layer of grayish material covered the under surface of the cerebellum over the middle and part of the lateral lobes, varying in thickness and extending for about half an inch into the nervous tissue. Middle lobe almost entirely replaced by a soft, gray, vascular growth. Pia-arachnoid over medulla and pons normal. Thin layer of new growth on left side of optic chiasm and nerve, with similar patch, about the size of a pea, on under surface of left lower temporal convolution. Lateral ventricles greatly distended. Basal ganglia normal. Spinal cord appeared enlarged at upper part with small scattered hæmorrhages in the gray matter. Posterior aspect of the cord covered throughout by new growth $\frac{1}{4}$ to $\frac{1}{2}$ inch thick in lumbar region. The tumor was a small round-celled sarcoma.

III. (Ollivier.†) Male, aged 11 years. Duration of disease about 6 months. There were paroxysmal headaches, retraction of head, convulsions, and later vomiting. Two days before death blindness with dilated pupils and pains in the limbs. The day before death acute pains throughout the body, but worst in the back; sensation and motion unimpaired. Patient conscious. Convulsions, constipation and nausea; no vomiting.

Autopsy.—There was a uniform pinkish formation extending over the posterior surface of the cord, averaging one line in thickness, thinner toward lateral aspects of the cord and blended with arachnoid. It was fairly firm, like unsoftened cerebral tissue, and traversed by small blood-vessels. There was a tumor in the cerebellum.

IV. (Hadden.‡) Although described as chronic cerebro-spinal meningitis, this case was evidently one of diffuse meningeal sarcoma. Male, aged 13 years. Duration 14 to 17 months. An injury to the head 17 months before death was followed by pain in the head and vom-

* *Trans. Path. Soc.*, London, xxxviii (1887), 26.

† *Traité des maladies de la moelle épinière*, t. ii, p. 490, obs. cxxxviii, Paris, 1837.

‡ *Trans. Path. Soc.*, London, xxxvi (1885), 13.

iting. 14 months before death sickness in the morning, pain in the head, fainting and attacks of dizziness. Two or three months before death weakness of legs, loss of control over bladder, convulsions, followed by stupor, occurring as frequently as 4 or 5 times a day and ceasing a few weeks before the fatal ending. The patient was drowsy and nearly blind, the pupils being equal, dilated and sluggish. Temperature usually normal or sub-normal, being only twice above 100° F.

Autopsy.—Under surface of cerebellum almost entirely coated with an opaque white material varying in thickness from 1 to 4 mm. Upper surface of cerebellum and adjacent parts of the cerebrum similarly but less extensively affected. Tips of temporosphenoidal lobes showed the same condition in a minor degree. Much thickening and white opacity about optic tracts and chiasm. Lateral ventricles distended with clear fluid. No tumor in the brain. Beneath arachnoid on posterior surface of lower dorsal and lumbar cord a thick, white layer similar to that upon cerebellum, which presented numerous bleb-like elevations. Cervical and upper dorsal cord free.

The white thickening over cerebellum and cord consisted microscopically of round and spindle-shaped cells with a considerable amount of new connective tissue in interlacing bundles. The vessels were large. No tubercles.

V. (E. L. Fox.*) Male, aged 29 years. Duration of disease not given (patient came to hospital after being sick for three months, and probably did not live long afterward); began with shooting pains in arms. Gradual flexion of fingers developed. Difficulty in urinating and priapism. On admission anæsthesia of legs, thighs, abdomen and chest to third rib, and paralysis of lower extremities.

Autopsy.—The cord seemed generally larger than normal with a marked swelling posteriorly at its upper portion midway between cervical bulb and second cervical vertebra. On section this was found to be a tumor, 1½ in. long and ¾ in. broad, with well-defined margins of a purplish color and tolerably firm. Cord smaller than normal, the great apparent increase in size being due to a layer of yellowish-gray substance fully ¼ in. thick, enveloping cord on all sides. This growth extended from highest portion of cord to cauda equina. In pia mater covering pons and medulla much thickening and rounded masses of exudate extending along the vessels as far as fissure of Sylvius.

Microscopically the tumor was a spindle-celled sarcoma.

* *Bristol Medico-Chirurg. Journ.*, i (1883), 104.

VI. (G. H. Bennett.*) Male, aged 48 years. Duration about 11½ months. Began with weakness in legs. No headache or other cerebral symptoms except dizziness. Vision good. Dull aching in back and lower limbs. For six weeks before death patient could not stand; suffered from constant severe pains in legs and from attacks of uncontrollable vomiting.

Autopsy.—Areas of softening in cerebrum and cerebellum. Pia mater of cord thickened, especially its posterior aspect, most marked below and gradually diminishing upward. Posteriorly, membrane studded throughout with round and oval, isolated and confluent, white nodules, varying in size from mustard seed to pea. These growths surrounded posterior roots. None visible to naked eye in front or laterally. The growth was a round-celled sarcoma.

VII. (Westphal.†) Female, aged 15 years. Duration a little over a month. At first headache, dizziness and pain in back, and two weeks later convulsions. Mind dull, pupils irregular, slight paresis, pain over spine on percussion, no choked disk. Before death severe headache, dizziness, vomiting, paralysis of ocular muscles and absence of knee-jerk. No fever. Death took place in a convulsion.

Autopsy.—Grayish-white and in parts more reddish thickening of pia-arachnoid, extending from optic chiasm backward over pons and medulla and outward somewhat over temporal lobes. Cranial nerves more or less imbedded in tumor thickening. Lateral ventricles contained blood-tinged fluid. In and near left optic thalamus three firm, smooth tumors of a red and grayish-white color, one being connected with tela choroidea. Pia-arachnoid of cord, especially posteriorly, presented grayish-red tumor growths, slight above, but increasing downward, becoming in dorsal region a prominent covering. Cord itself normal. Metastatic nodules in lung.

The tumor was a richly nuclear, round-celled sarcoma, with numerous vessels scattered between the cells. The cord was not invaded. The spinal nerve-roots were imbedded in but not invaded by the growth. The tumor had implicated the cranial nerves.

VIII. (Virchow.‡) Male, aged 30, copper-worker; attacks of colic, paresis and toward the last almost total blindness.

Autopsy.—On surface of hemisphere single yellowish-brown pigment spots. At base of brain a more diffuse, confluent deposit in the soft membranes of a melanotic material, extending laterally and thickest be-

* *Trans. Clin. Soc.*, London, xviii (1885), 168.

† *Arch. f. Psychiatrie*, xxvi (1894), 770.

‡ *Virchow's Archiv*, xvi (1859), 180.

tween chiasm and pons. At apex of middle lobe and on sides and middle of cerebellum growths as much as 3 lines in thickness. Diffuse growth along various cranial nerves, optic and olfactory being imbedded in it. The growth extended into the nerves and completely infiltrated the Gasserian ganglion, but did not extend beyond the foramina. Eyes normal. On posterior surface of cord in upper part isolated, flat, almost black tumors; below in dorsal and lumbar regions these became continuous, the cord being covered by a layer of growth 2 to 3 lines thick. In cervical portion, posteriorly and laterally and in front throughout, only blackish-brown pigmentation was apparent. Nerves of cauda equina and most of other spinal nerves covered by growth forming in places nodules. The tumor was a round and spindle-celled melanotic sarcoma. In a few places pigment was absent.

IX. (G. Lentz.*) Male, aged 23 years. Duration about 12 months. Began with pain in back, later in arms and legs; weakness of muscles, first in legs, later in arms and trunk. At end of 6 months pain and tenderness on percussion over spine and exaggerated patellar reflexes. Optic neuritis with normal pupillary reaction. One month before death patient was bed-ridden, mind dull, pupils irregular and sluggish, bilateral choked disk, marked paresis and atrophy of muscles. Patellar reflex present on right side only. Sensibility reduced in legs, arms and parts of back. Later vomiting and cystitis.

Autopsy.—There was a tumor involving corpus callosum and laterally invading the hemisphere. Lateral ventricles distended with fluid. A cavity in upper part of cord. Whole posterior extent of cord covered by a pale gray mass about 1 mm. thick. In dorsal region growth extended to the sides of cord. From lumbar region downward whole cord encased in a gray, homogeneous, jelly-like mass 0.5 cm. thick. Cord was of normal appearance only in the lower portion.

The mass of the tumor consisted of closely-packed, short, oval or roundish cells, separated by scanty interstitial tissue, in places distinctly fibrillated. There were abundant vessels with well-developed walls, some having undergone hyaline changes. The pia was usually sharply differentiated from the cord, and in places the tumor penetrated along the pial septa. Here and there the connective tissue was arranged so as to form a meshwork in the spaces of which the cells were accumulated. Large cells of endothelial type were found singly and at times in groups. Limited portions of cord were directly invaded by the tumor. The cerebral tumor was of similar structure and hæmorrhagic.

* Ziegler's *Beiträge*, xix (1896), 663.

X. (R. Schulz.*) Female, aged 16 years. Duration about 3 months. Severe pain in back, numbness and formication in hands and arms, with increasing weakness in arms, which were paralyzed shortly before death. Patient conscious up to the last. Pain in head, nutrition good, inability to stand, hands red and swollen, tenderness on pressure over main nerves of trunk and upper limbs. No affection of cerebral nerves. Marked tenderness over whole spine, retention of urine, constipation; anæsthesia of both upper limbs and absence of the patellar reflex on right side. Clinical diagnosis was acute meningo-myelitis.

Autopsy.—Cranium and its contents normal. On opening spinal dura cord bulged, presenting a sausage-like appearance. Sub-arachnoid space occupied throughout by grayish-red mass of growth, covered by delicate arachnoid, nodular and lobulated, partly firm, in places soft and studded with hæmorrhages. In lumbar and lower dorsal regions growth completely ensheathed cord, while in the upper part it covered only posterior surface. At one point it penetrated the cord.

Microscopically growth was made up of large endothelial cells, traversed by numerous capillaries which gave it an alveolar character. It is described as an alveolar sarcoma.

Of the 11 cases, including the one here reported, in which there was a diffuse sarcomatous growth in the pia mater of the cord and base of the brain, in 6 there was no tumor of the nervous structures which could be considered primary (Coupland and Pasteur, Schulz, Hadden, Fox, Virchow). In the other five there was tumor growth in either the cerebrum, cerebellum, pons or basal ganglia. In all of these cases the macroscopic characteristics were very similar, as was also the distribution. In the cranial pia mater the growth was most abundant about the optic commissure and over the cerebellum, and spread here and there to the surface of the lower portions of the cerebrum. It usually extended more or less along the cranial nerves. The spinal growth was most extensive along the posterior surface of the lower part of the cord. The posterior growth was comparatively slight in the upper part, as was also that in front and to the sides of the cord throughout the entire length. The tumor tissue was yellowish or grayish-white, with more or less of a pink or red color in some cases. The consistence varied, but was usually rather soft.

* *Archiv f. Psych.*, xvi (1885), 592. (Abs. in *Trans. Path. Soc.*, London, xxxviii (1887), 32.)

The microscopic characters of the tumors from the various cases have differed somewhat. Virchow's case is the only one of a melanotic growth. Schulz reports his case as one of alveolar sarcoma. In Hadden's case the tumor is said to consist of round and spindle cells, and Fox's was one of spindle-cell growth. In the two cases of Coupland and Pasteur, in those of Bennett, Lentz and Westphal, and in my case, the tumor was a small, round-celled sarcoma. In some of the cases the blood-vessels are spoken of as being large and abundant. There was usually little or no tendency for the growth to invade contiguous structures. The cord was rarely involved, and then only to a slight degree; the brain was more apt to suffer. The growth, however, showed a special tendency to infiltrate the pia mater even to its finest processes and prolongations. The cranial nerves were occasionally invaded by the tumor cells, but the spinal nerve-roots, even when imbedded in a mass of tumor tissue, were only occasionally directly attacked.

The variety of diagnoses made *intra vitam* in the reported cases indicates the divergent character of the clinical manifestations. This is largely due to the wide diffusion of the lesions and the association in many of the cases of symptoms produced by one or more tumor nodules in the brain. In my case the large growths in the cerebrum and fourth ventricle had not given rise to symptoms, and it was thought by the clinicians who had studied the case that localized tumor could be excluded from the diagnosis.

The ages of the patients varied from $4\frac{1}{2}$ to 48 years. Of those in which the age is recorded, 6 were under 20 years and only one above 30 years. The course was usually tolerably rapid, the fatal termination being reached within a few months. Pain in the head and back was an early symptom. There were often pain and hyperæsthesia in the extremities, followed by muscular weakness, and later paralysis. Constipation was sometimes followed by incontinence of fæces and urine. Paralysis of the ocular muscles, partial or complete loss of sight and optic neuritis were noted. The temperature was not usually above the normal. In the early stages consciousness was often unimpaired, but later was sometimes much disturbed.