

# LESIONS IN THE MIDBRAIN

## REPORT OF A CASE

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Although the midbrain is one of the smallest divisions of the central nervous system, within its structure are to be found certain essential nuclear centers and great nerve paths, motor and sensory, connecting the cerebrum and cerebellum with the spinal cord and thence with the entire nervous system. It is the continuation upward from the pons varioli and comprises the two crura of the cerebrum which are surmounted by two pairs of tubercles; the corpora quadrigemina. The aqueduct of Sylvius, connecting the third and fourth ventricles, penetrates its entire length on its dorsal aspect.

Its principal nuclear structures, in addition to the quadrigeminal bodies, are the two large paired red nuclei, receiving fibers from the superior cerebellar peduncles, the nuclei of the third and fourth cranial nerves, the central gray nuclei, the small nuclei of the fifth nerve, the nuclei of the posterior commissure of the posterior longitudinal bundles and the substantia nigra. At its upper border the midbrain is in close relation to the thalamus and the geniculate bodies.

Because of its central position and of the compactness of its structure, the region of the midbrain presents a difficult field for experimental study. The changes, therefore, in this area brought about by injury and disease have furnished more important information of the function of the several elements composing the midbrain. Extensive lesions in the midbrain are difficult to interpret because of the many complicated connections involved.

The topical diagnosis of lesions in this area has been exhaustively treated by Marburg.<sup>1</sup> Many of the deductions from the reported cases are somewhat conjectural. It is difficult, of course, to distinguish between symptoms that may be due to the destruction of nerve tissue by disease and those which are produced by alteration in function in the same area because of the involvement of neighboring structures. From the mass of often confusing data three more or less outstanding syndromes have emerged as the result of disease in various portions of the midbrain. These are:

(a) Syndrome of Weber,<sup>2</sup> which consists of hemiplegia in one side of the body with oculomotor palsy of the other side. This results

1. Marburg: *Wien. klin. Wchnschr.* **18**:532, 1905.

2. Weber: *Med. Chir. Trans.*, 1863, cited by Jelliffe and White: *Dis. Nerv. System*, Ed. 3, p. 542, 1919.

from a lesion affecting one of the peduncles, due usually to thrombosis of the basilar artery, to tumors or to inflammatory products in this region, and extending mediumly so as to compress the third cranial nerve or its nucleus.

(b) Syndrome of Benedict,<sup>3</sup> which consists of the Weber syndrome plus a tremor on the side of the hemiplegia, that is, some oculomotor palsy with a crossed hemiplegia and a persistent tremor which increases somewhat on voluntary motion. Apparently, there is some uncertainty as to the site of this lesion but it probably represents the involvement of the peduncle and the third nerve, the lesion also reaching dorsally to the red nucleus which receives nerve fibers directly from the cerebellum. If the lesion fails to involve the peduncles the hemiplegia may be absent.

(c) Syndrome of Nothnagel,<sup>4</sup> which is described as a unilateral or bilateral oculomotor palsy with ataxia of the cerebellum type. It is supposed to suggest the lesion of the corpora quadrigemina with pressure upon the superior cerebellar peduncles. Symptoms of this character are more often the result of tumor in the corpora quadrigemina or in the pineal gland.

In view of the confusing symptomatology often noted in patients suffering from midbrain lesion it will be of interest to report a case in which the symptoms were comparatively definite and the pathologic findings fairly circumscribed.

#### REPORT OF CASE

The patient was a colored boy; R. J. [No. 6747], 3 years of age who was brought to the Harriet Lane Home, Johns Hopkins Hospital, Feb. 3, 1915, because of "general weakness and trembling and drooping of the eyelids."

*Family History.*—The family history was negative; the father and mother were well; one sister and one brother were living and well; a brother died of pneumonia at 10 months. There had been no other pregnancies and no history of syphilis or tuberculosis or of any illness in the family similar to that of the patient.

*Personal History.*—The child was born at full term without instruments and was breast fed for fourteen months. He had measles at 18 months and pertussis at 2½ years with uninterrupted recoveries. There have been no other illnesses and no sore throat or skin eruptions. The boy's development was normal. He cut his first teeth at 4 months, walked well at 11 months and talked at 17 months. There have been no disturbances of digestion and no renal symptoms.

The patient appeared to be perfectly normal until six months before admission when he stopped crying almost completely. Nothing further unusual was noted, however, until four months afterward when it was noted that his hands would shake when feeding himself. No paralysis or weakness had been

3. Benedict: *Nerv. Pathol.*, 1872, cited by Jelliffe: *Interstate M. J.* **18**:819, 1911.

4. Nothnagel: *Brain* (July) 1889; cited by Marburg.

remarked up to this time. At about the same period and following a coryza the mother noticed that the boy's eyes began to droop; both sides were equally affected. The child became nervous, jumped at every noise but no other change was observed except that he did not cry. The mother thought him "as bright as before."

*Physical Examination.*—When seen the child's general condition seemed excellent. His temperature was 99.6 F.; the skin was clear; his head was well formed; the circumference being 19½ inches. The fontanels were closed. No abnormalities were detected about nose, ears or throat. The teeth were in excellent condition. There was some enlargement of the epitrochlear glands.

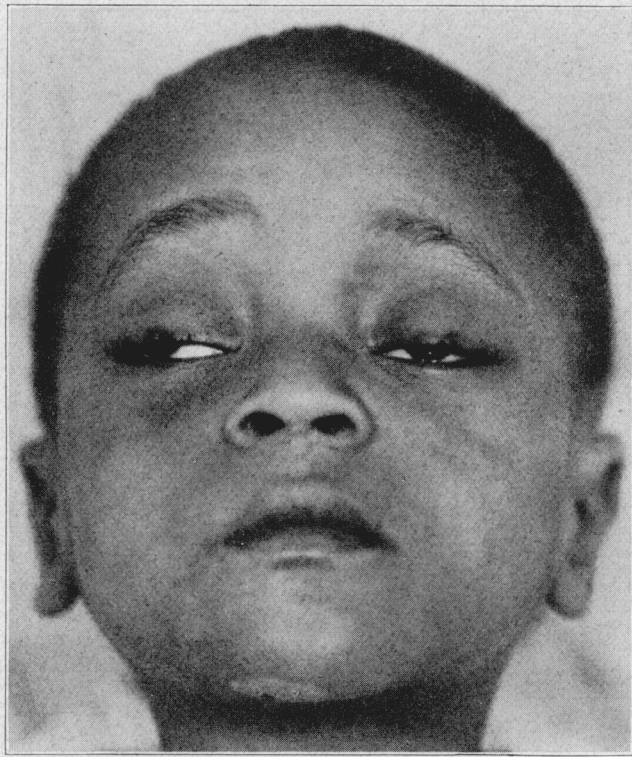


Fig. 1.—Bilateral ptosis and external strabismus of right eye due to unbalanced action of external oblique muscle.

*Eyes:* The pupils reacted to light, the left better than the right. There was an occasional lateral nystagmus of the right eye. A marked bilateral ptosis of the eyelids, apparently equal on both sides, was present. There was definite lateral deviation of the eyeballs to the right. Upward deviation was not well observed; downward deviation seemed normal. There was no conjunctivitis or photophobia.

The lungs, heart and abdomen presented no abnormalities. No definite weakness of the muscles of the legs or arms could be shown—sensation was normal. No alteration was found in the deep reflexes, except that those at the knee were somewhat increased. His gait seemed normal and he executed

the finer movements well. Romberg's sign was absent. The boy seemed unusually bright. He obeyed commands well and was not irritable. The Wassermann reaction was negative.

*Later Examination.*—Two weeks later the patient returned with the history of having had two attacks of weakness (paraplegia), and that he had become very weak and limp after the second one. He was admitted to the ward, February 18. Three days afterward he became somewhat drowsy and difficult to arouse. Macewen's sign was suggestive. There was an increase of ptosis of the right eyelid which he could not raise as well as the left.

When placed on the floor, he stood with his head thrown back, arms outstretched and the feet far apart. When attempting to walk there was great uncertainty of movement and when standing or walking there was a coarse tremor of both arms and legs.

There was no movement of the eyeballs, excepting those produced by the action of the external recti. The examination of the fundi showed a very slight degree of secondary atrophy. There was no evident impairment of hearing.

*Laboratory Examination.*—The spinal fluid obtained was under a marked increase in pressure, gave a reaction for globulin and contained an increased number of cells mostly of the mononuclear type. On subsequent examinations the number of cells increased from 38 to 200 per c.mm. The Wassermann reaction in the blood and spinal fluid were negative. The von Pirquet test was frankly positive.

*Roentgenoscopy.*—The roentgen-ray examination of the head showed a moderate internal hydrocephalus and a probable tumor above the sella turcica. March 1, ten days after admission, a slight rigidity of the neck was noticed for the first time and from this time on the child grew constantly weaker. He was no longer able to support his weight on his feet. His respirations became shallow and irregular. There were slight daily fluctuations of temperature of about  $2\frac{1}{2}$  degrees. The external strabismus of the right eye became more marked; the ptosis continued more prominent in the right eye than in the left eye—the pupils reacted slightly to light. The ataxic movements of the hand were still noted when the child attempted to reach for objects.

The drowsiness gradually deepened. March 9, he had the first of a series of general convulsions, which continued daily until his removal from the hospital against advice March 15. No tubercle bacilli were found in the spinal fluid on repeated examinations.

He died at his home March 18, after being under observation forty-two days.

*Comment.*—The acquired ptosis and the curious tremor of long standing noted in the extremities and the gradually developing paralysis of the movements of the eyeballs excepting those produced by the external recti, with resulting external strabismus, occurring spontaneously in a child previously well, lead one to venture the diagnosis of tumor of the midbrain, interfering with the nuclei of the third and fourth cranial nerves. The ataxia might also be accounted for by lesion in this area, involving the red nucleus or cerebellar tracts. Toward the end there was certainly meningitis, probably of tuberculous origin, associated with hydrocephalus, although the tubercle bacilli were not demonstrated. The positive von Pirquet reaction and the subsequent development of meningitis suggested that the initial lesion in the midbrain was probably tuberculous in origin.

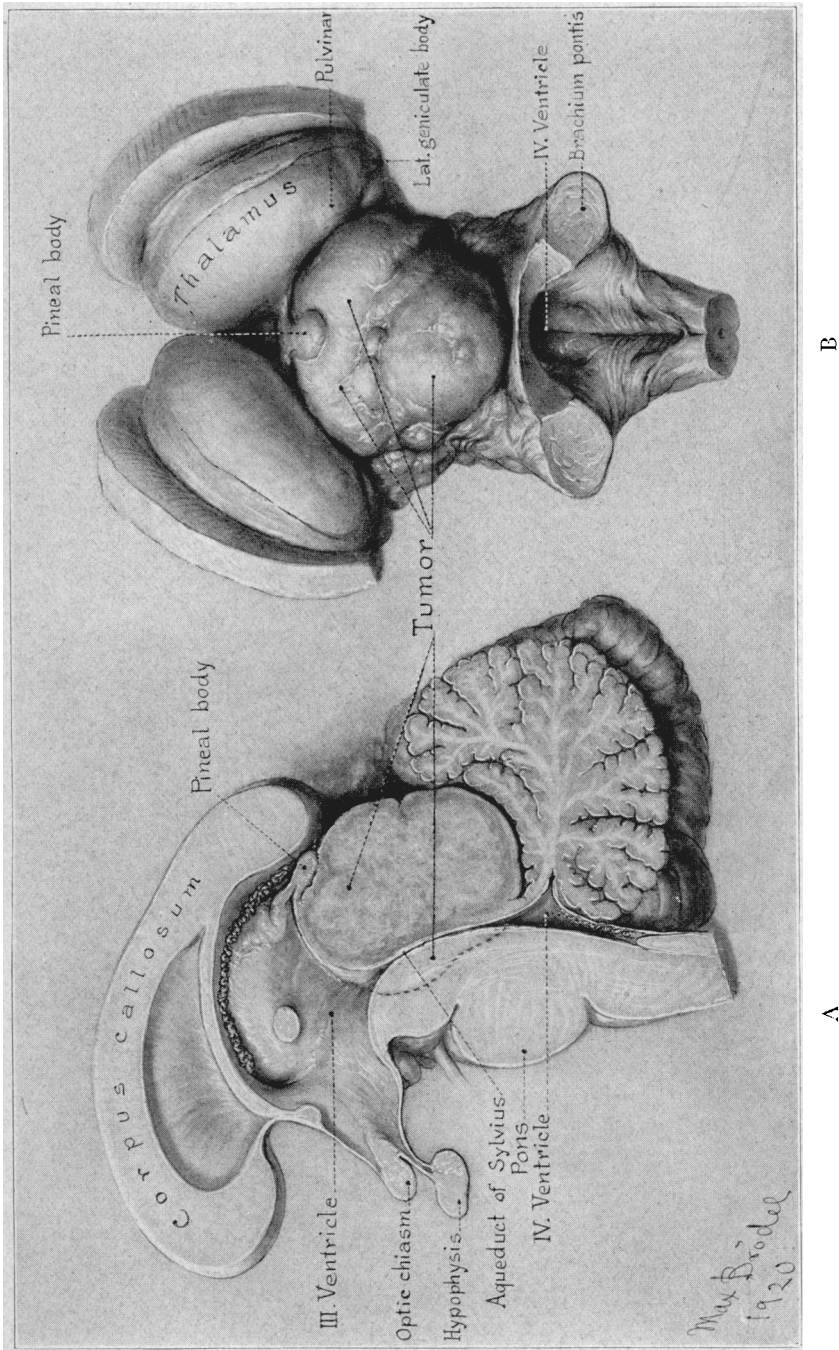


Fig. 2.—A. Sagittal section, showing the extent of the tumor, narrowing but not occluding the aqueduct of Sylvius. Most of the growth is on the right of the median line. The pineal gland is not involved. B. Sketch of the roof of the midbrain showing the displacement of the colliculi by the tumor and its relation to the thalamus and pons.

Necropsy 4310. March 19, 1915. Dr. Holmes:

A plastic exudate was found over the base of the brain, extending up to the roof of the fourth ventricle; fine tubercles were seen along the course of the blood vessels about the base and on the surface of the cerebellum. A solitary tubercle, 0.6 cm. in diameter, surrounded by a reddened zone, the whole having a diameter of 1 cm. was found in the tip of the temporal lobe. Dissection of the brain stem disclosed a large tubercle the size of a hickory nut which took the place of the upper surface of the midbrain, the colliculi. The foramen of Magendie was patent, but the surrounding cisternae were plastered down by exudate. The velum intrapositum was thickened, especially on the right.

I am indebted to Dr. Adolf Meyer for the following description, gross and microscopic, of the tumor:

#### REPORT ON EXAMINATION OF TUMOR

The tumor of the midbrain extends backward and inflates the whole roof so that the frenulum disappears and the two fourth nerves come out from the side of the tumor. On the forward side, the tumor has a thickness of about 18 mm., while the breadth is about 32 mm. The anterior end raises the epithalamus and superior commissure, pineal gland and pineal recess exactly 10 mm. from the transverse ridge of the posterior commissure. The midbrain ventricle is only compressed but not occluded. The whole region was cut horizontally so as to expose the third nucleus of each side.

*Microscopic Description.*—The tumor at a level just underneath the midbrain or aqueduct takes up nearly the whole right side of the midbrain from close to the median line to the region of the lateral fillet. In the posterior part some motor cells are preserved in tissue partly invaded by the tubercle (region of fourth nucleus) but the more anterior part of the third nucleus is invaded and completely destroyed.

The left third nucleus is not invaded, at least not in its more lateral part. There is no evidence of clean cut and limited destruction of any portion which could be made responsible for the ptosis of that side. It is more likely that we have to account for the motor restriction by pressure. Practically all the cells show dissociation of the Nissl bodies of the nature of fever alteration which reduces the possibility of distinguishing the normal and abnormal cells. Below the level just described the tumor terminates above the red nucleus without, however, invading it definitely.

In the central part of the tumor there are diffuse islands which have lost all nuclei. Only along the blood vessels are there evidences of cellular infiltration and residual tubercles. In the more superficial part of the tumor there is less necrosis and there is a fairly large number of characteristic giant cells. Tubercle bacilli could not be stained in the rather old specimen. On the surface the pia shows meningitis infiltration.

The anatomic diagnosis is solitary tubercle of the midbrain and right parietal lobe, tuberculous meningitis.

*Comment.*—The anatomic findings confirm, in the main, the clinical diagnosis and account for the symptoms present, although the bilateral character of the ptosis and the paralysis of the ocular muscles would have been more easily accounted for if the destruction of the third and fourth nuclei could have been demonstrated on both sides. However, a mass of the size described must exert marked pressure with interference of function in the adjacent structures not directly involved.

in the tumor. This fact with the well known collateral connections between the oculomotor tracts may satisfactorily account for the bilateral symptoms. In regard to the ataxia tremor, it is unwise to make any dogmatic statement in the presence of tubercular meningitis with increased cranial pressure. As, however, the peculiar ataxic tremor of the hands was noticed among the very early symptoms, it is not unlikely that they were produced by the primary lesion, the tuberculoma in the midbrain.

The general weakness and ataxic gait which came on later were probably the result of the meningitis and increased cerebral pressure.

The occurrence of tremors in cerebral lesions has been discussed by Gordon Holmes.<sup>5</sup> From data from sixty cases with necropsy findings he concludes that the movements are athetoid when the thalamus is involved, are chronic when the midbrain and ganglia are involved and true tremor when the lesion is in the midbrain itself.

Jelliffe<sup>6</sup> considers that choreiform and chorei-ataxic movements are the result of a lesion in the midbrain with the involvement of the superior cerebellar peduncles, whereas those tremors suggesting paralysis agitans arise from involvement of the red nucleus.

It would seem more probable that the choreo-ataxic tremor noted in my case might be associated with involvement of the superior cerebellar peduncles, as the growth itself did not reach the red nucleus.

Tumors limited strictly to the corpora quadrigeminal bodies must be extremely rare. The symptoms produced by a growth beginning in this area are due to the involvement of the underlying structures.

Ferrier and Turner<sup>7</sup> have shown that destruction of those bodies in monkeys does not result in any permanent phenomena and that the colliculae themselves apparently have a small functional value.

Among the rather infrequent cases, similar to mine in the literature should be mentioned those of Nissen,<sup>8</sup> who out of the large clinical material of Elizabeth Hospital, St. Petersburg, has reported five cases in which the diagnosis of tubercle of the midbrain was made and in three confirmed at necropsy. In the first case, a boy of 3 years, the principal symptoms were a gradually increasing ptosis of the right eyelid—later of both sides—oculomotor paralysis becoming complete, and a spastic paralysis of the left extremities. On section there was found a large caseous mass in the right side of the midbrain, involving the cerebral peduncle and extending nearly to the roof so as to invade the oculomotor nuclei. There was no meningitis and only moderate hydrocephalus.

5. Holmes, G.: *Brain* **27**:327, 1904.

6. Jelliffe: *Interstate M. J.* **18**:817, 1911.

7. Ferrier and Turner: *Brain* **24**:27, 1901.

8. Nissen: *Jahrb. f. Kinderh.* **54**:618, 1901.

In the second case, a child 19 months old, certain additional symptoms were noted, namely, some stiffness of the neck and diminution of vision. These were explained by pressure in the medulla and by the extension of the caseous tumor into the optic thalamus.

The fifth case, a child 5 years old, had symptoms suggesting a tuberculosis of the brain with paralysis of both sixth nerves and optic neuritis. At necropsy an extensive tuberculous exudate involving the sixth nerves was found and complete destruction by caseous material of the corpora quadrigemina, to which no definite symptoms could be attributed.

Nissen is of the opinion that tumors of the midbrain proper tend in their earlier stages to produce only localized effects, that the general symptoms of brain tumor referable to increased intracranial pressure, such as headache, vertigo and optic atrophy, are more prone to follow tumors in other parts of the brain. He calls attention to the fact that several tuberculous masses are twice as likely to occur in the brain as is a single solitary tubercle.

Hoppe<sup>9</sup> has reported a case of a girl, 17 years of age, who died after an illness of a year as the result of a tumor in about the same situation as that of our patient. The principal symptoms were headache, double vision, ending in four months in total blindness; ataxia, staggering gait, paralysis of the external recti of both eyes, slight ptosis of both eyelids and atrophy of the optic nerve. There was no defect in hearing or alteration in sensation. On necropsy, a gliomatous mass, 2 by 4 cm., was found involving the corpora quadrigemina and extending back into the left cerebellar hemisphere. The nuclei of the third and fourth cranial nerves were involved but the blindness was due probably to the papilledema of the optic nerve brought about by the increased intracranial pressure. This hypertension also exerted on the nerve trunk of the sixth nerve might explain the paralysis of the external recti. This case confirms the experimental evidence and the contention of Nissen and others that neither blindness, deafness, nor ataxia are pathognomonic of the disturbed function of the quadrigemina.

Another important structure in close proximity to the midbrain must be considered briefly, namely, the pineal gland, which lies immediately upon the anterior corpora quadrigemina.

The pineal gland is the seat not infrequently of hypertrophy, tumors, cysts and various degenerative changes which may exert pressure on the subjacent structures. The quadrigeminal bodies may be flattened or destroyed and the whole midbrain greatly distorted by these masses springing from the pineal gland.

9. Hoppe: *J. Nerv. & Ment. Dis.* **39**:108, 1912.



The anatomy, physiology and pathology of the pineal body has been extensively studied. Bailey and Jelliffe<sup>10</sup> have collected a large series of tumors of the pineal gland and Kidd<sup>11</sup> in 1913 summarized all the data bearing upon the body. These writers and Skoog<sup>12</sup> discuss the metabolic changes which may reside in the pineal gland.

It has been claimed that adiposity and the development of premature sexual characteristics result from interference with the function of the pineal gland. The reference of these changes directly to the pineal body must be accepted with reserve, as Park<sup>13</sup> has pointed out that of the seventy cases of pineal gland tumors reported symptoms of precocious development appear in but five and excessive growth in but seven, and that it is quite possible that the occasional results may be due to secondary alterations of neighboring structures, as for example the pituitary.

The neurologic signs and symptoms, however, resulting from pineal tumor must be considered in discussing the affections of midbrain injury. Among them are headache, increased intracranial pressure, often with hydrocephalus, giddiness, nausea, drowsiness, isolated eye palsies, ataxic gait and tremor. It is evident that many of these symptoms are identical with those produced by primary lesions of the midbrain.

The order in which certain localizing symptoms develop is of the utmost importance in reaching an accurate diagnosis. When the early symptoms are general and attributable to increased cerebral pressure, such as headache, vomiting, optic atrophy, hydrocephalus, etc., followed, perhaps, by ptosis and oculomotor palsies, one would be inclined to place the initial lesion outside of the midbrain—such symptoms might result from meningitis or tumor elsewhere, possibly originating in the pineal gland. Whereas, as in the case here reported, the limitation of the symptoms for months to ptosis and paralysis of the oculomotor nerves and tremor without evidence of increased intracranial pressure support the diagnosis of an injury beginning in the midbrain, and as far as it goes, the absence in my case of any increased rate of growth or of sexual development suggest that neither the pineal nor pituitary glands were involved.

I take pleasure in thanking Dr. Adolf Meyer for his kindly interest and assistance in describing the specimen, and Dr. John Howland for the opportunity of reporting the case from his wards, and Mr. Max Broedel for the accurate drawings.

10. Bailey and Jelliffe: *Arch. Int. Med.* **8**:851 (Dec.) 1911.

11. Kidd: *Neurol. & Psychol.* **11**:1, 1913.

12. Skoog: *Tr. Sect. Nerv. & Ment. Dis., A. M. A.*, 1918, p. 241.

13. Park: *Am. J. Dis. Child.* **12**:477 (Oct.) 1916.