CEREBRAL PALSIES WITHOUT DEMONSTRABLE ANATOMICAL FINDINGS¹

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Cases of cerebral palsies without demonstrable lesion in the brain and without implication of the pyramidal tracts have been frequently reported. The cases however have by no means a common pathology. Perhaps the most usual form of these palsies consists of hemiplegia of toxic origin, such as those that occur after or during nephritis (Jacobson (1), Brodier (2) and others); or during pulmonary tuberculosis, pneumonia or as the result of lead poisoning and puerperal infection (Jacobson), or in alcoholics (Eichorst (3)). They may be also the result of disturbances of the circulation consisting of changes in blood vessels (Hochhaus (4) and Wernicke (5)); or due to vasomotor disturbance of toxic origin causing fugacious edemas (Le Calvé (6)).

While the aim of this paper is to call attention especially to the cases of infantile cerebral palsies without a clear-cut demonstrable lesion it is impossible to exclude from brief reference, for the purpose of elucidation, these cases, as well as those in which a lesion of the brain is found but in which at the same time no degeneration of the pyramidal tracts can be demonstrated. Such for example are the cases reported by Binswanger (7), Babinski (8) and Oppenheim (9), in which tumors of the brain have caused paralysis but in which degeneration of the pyramidal tracts has been lacking.

In addition to these there is also a group of cases of hemiplegia without disease of the pyramidal tracts in which is found in the

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basil ganglia a lesion consisting of lacunae described by Marie (10) under the name of *état criblé*, instances of which have been reported by Mikulski (11). In this group may be included the cases exhibiting lesions of the temporal lobe (Mikulski), of the lenticular nucleus (Wilson (12) and Oppenheim (13)), of the caudate nucleus and optic thalamus (Hoestermann (14)), of the optic thalamus (Bischoff (15), Nothnagel (16), Wernicke (17) and Oppenheim (18)) and the case cited by Marie and Guillaîne (19) of lesion of the red nucleus with secondary degeneration of the tegmentum, the cerebellar peduncle, and posterior longitudinal bundle.

There is then beside these a large group of cases that are described as infantile cerebral palsies in which the symptoms are characteristic and comparatively uniform in which again however the pathology is varied.

Excluding the cases of porencephalon and atrophy in the motor and other regions, associated with degeneration of the pyramidal tracts there is a comparatively small number of cases on record in which there is little or no demonstrable lesion either in the cortex or the motor tracts of the spinal cord.

In a number of these cases no true degeneration is found in the pyramidal tracts but a fineness of the fibers (Spiller (20), Binswanger (21)); or a scarcity of fiber (Ganghofer (22)), or incomplete myelination of the fibers (Haushalter & Collins (23)), or agenesis or imperfect development of the pyramidal tracts (Spiller (24), Ganghofer, Steinlechner-Gretschischnikoff (25) and Otto (26)), or finally atrophy of the pyramidal tracts (Ganghofer, Steinlechner-Gretschischnikoff).

Cellular changes in the cortex more or less marked have been described in some cases, the exact significance of which I believe is still open to discussion.

In Otto's cases there was a lack of development of the cortical cells especially the large pyramidal cells, and an entire absence of Betz cells. The absence of secondary degeneration in the pyramidal tracts is difficult to explain in this case if we accept as true that the fibers of the pyramidal tracts are directly connected with the Betz cells.

In one of Rolly's (27) cases there was some ganglion cell degeneration of moderate grade, added to proliferation of the glia

and small vessels. Otherwise except for a slight external hydrocephalus there was nothing abnormal.

In some of the cases the cells of the cortex show little or no change. In a second case cited by Rolly of bilateral spasticity in a child who died at the age of 2 months there was nothing pathological except a proliferation of the glia and blood vessels.

In Haushalter and Collin's case there was no abnormality of the Rolandic cortex and the pyramidal tracts were normal except for incomplete myelination.

In Ganghofer's case the findings were negative except in one there was a scarcity of fibers observed.

In the three cases described by Spiller very slight pathological changes were found. In one of his cases an idiot with contracture of the feet, and inability to support the body or to use the hands, the brain showed no gross lesions. The Betz cells were not numerous and were smaller than normal and the fibers of the pyramidal tracts were remarkably fine.

In a second case, an idiot who could not talk, walk, or support his body and who was probably spastic and had increased reflexes in the legs but not in the arms which could be used, there was no gross or microscopic change in the brain or cord.

The third case was that of a girl who could not walk or talk, nor could she use the hands in voluntary effort. The Betz cells were numerous and showed change which may have been due to post mortem degeneration. The cells of the spinal cord were normal. The fibers of the crossed pyramidal tracts of the cervical region were very fine and finer than the columns of Goll or of the pyramidal tracts in a normal child of the same age.

This case he looked upon as one of agenesis of the pyramidal tracts as was true he believed of his first case. In his second case he inclined to the belief that the nerve fibers in the pyramidal tracts "had not grown downward into the cord in normal numbers so far as the lumbar region, although the cervical region was well supplied."

Railton (28) described a case of spastic hemiplegia in an idiot of 3 years in which there was a depression forming a shallow groove parallel with and involving the fissure of Rolando. Microscopically the pons, medulla and cord were perfectly normal.

There was some diminution in the number of the large ganglia cells and increase in the neuroglia only.

More recently changes in the cells have been noted by Finkelnberg (29), Spielmeyer (30) and Hoestermann which they believe explain the cause of the paralysis as well as the preservation of the pyramidal tracts in these cases.

Finkelnberg's case was one of infantile spastic paraplegia which beside a moderate degree of hydrocephalus showed the presence of an atrophy of the cortex in the motor region with preservation of the large ganglion cells (*Riesenpyramidenzellen*) and in which secondary degeneration of the pyramidal tracts was absent. The cells in the cortex in the first to the fourth layers were diminished in number and irregularly arranged, while the Betz cells were normal. He did not believe that the hydrocephalus explained the degeneration of the cortex but believed that the atrophy of the cortical layer produced a functional disturbance affecting the motor conductivity, at the same time leaving the trophic influence intact.

Hoestermann cited a case of spastic diplegia in a woman of 34 years who had been an idiot and an epileptic since birth in which there was porencephalon of the right occipital lobe and some atrophy of the entire right hemisphere. There was a sclerotic atrophy of a great part of the cortex in the temporal, parietal, and occipital lobes. The spinal cord was practically intact.

In the cortex there was an irregular placing of the small pyramidal cells extending from the layer of the large ganglion cells to the molecular layer, consisting of a slight atrophy of the cells generally but which was very intense in the molecular layer. The large ganglion cells showed some irregularity but were in a normal position on the right side though not on the left. The pyramids in the medulla oblongata were normal except the left which was slightly lighter in color than the right. The von Monakow's bundle was not diseased.

In a second case of idiocy with convulsions, left-sided spastic palsy and inability to walk or talk, there was found microgyria. The small pyramidal cells in the right central convolution were reduced in number and were irregularly placed. There was no diminution in the large ganglion cells and these were normal. The left central convolutions were normal.

The left pyramidal tract was smaller than the right and smaller in proportion than the posterior columns, while the left anterior horns of the spinal cord were smaller than the right and poor in ganglion cells.

In a third case of Hoestermann, a young man, with strabismus, left hemiplegia, spasticity and increased reflexes, the left hemisphere was slightly larger than normal and there was a porencephalic defect in the right temporal, occipital and frontal regions. The cortex in all its layers was poor in cells, particularly the molecular layers, while the small pyramidal cells were increased in number. The ganglion cells were present but were less numerous than normal. The spinal cord was intact.

In a fourth case of paralysis of all members in a girl of 9 years gradually developing since 4 years of age there was external hydrocephalus, hemorrhage in the right caudate nucleus and in the right optic thalamus of old date. There were, besides, irregular orientation of the pyramidal cells in the central convolution and almost complete disappearance of the fibers of the cortex as shown by the Weigert method.

The cord was negative except for an embryonal type of the anterior pyramidal tract in the thoracic region and a paleness of Helweg's triangular field in the cervical region.

Hoestermann believed that the atrophy of the cells in the upper layers of the cortex caused palsy while the preservation of the lower layers guaranteed intactness of the trophic influence upon the pyramidal tracts.

Spielmeyer described a case of hemiplegia dating 2 years before death. The right hemisphere weighed 200 grams less than the left. The red nucleus, the optic thalamus on the right side and the left side of the cerebellum were reduced in volume and showed evidences of secondary atrophy. The pyramidal tracts in the spinal cord were intact.

In the cortex on the right side the cells of the cellular layer to the depth of the third zone were completely absent but in the deep layers a few cells were seen. There were also some large and middle sized cells in the third layer but the large ganglion cells showed no difference on the two sides.

In a former paper (31) I reported a case of spastic paraplegia (Case 1) dating from childhood, in a patient who died at the age

of 72 years. At the autopsy nothing was found abnormal macroscopically. A microscopic study of the cortex, pons, medulla oblongata, and spinal cord showed nothing pathological. The cells of the cortex appeared to be normal although no Betz cells were found in the sections from the paracentral region. In the spinal cord no degeneration was present and the examination was negative except for a fineness of the fibers of the crossed pyramidal tracts.

I shall in this report add two other cases, one of which was briefly presented to the Philadelphia Neurological Society on March 25, 1910 (35) and one for the privilege of reporting which I am indebted to Drs. Charles Frazier and William G. Spiller.

CASE 2.—L. S. was admitted to the Philadelphia Home for Incurables May 12, 1895, and died October 26, 1909, at the age of 27. The family history was lacking, except that a brother and sister were healthy.

At the time of her admission she stated that she had been suffering from jerky movements as long as she could remember.

Examination made at the time of her admission resulted as follows: There were constant involuntary movements, choreiform in character in arms and legs and face and more marked on the left side. Any attempt at voluntary effort increased the movements. The left hand was in constant motion. The legs were rigid, especially the left, which could not be extended beyond a right angle. There was distinct weakness of both the left arm and leg. The grip in the right hand was much stronger than in the left. There was no palsy of the face, and the tongue protruded straight and in the median line.

The knee jerk was increased on the right side but could not be elicited on the left side on account of the rigidity. There was an attempt at ankle clonus on the right side.

The pupils were equal and reacted to light. The speech was a little hesitating. She walked with distinct weakness of the left leg, the weight of the body coming down on the left toe.

The patient was undersized and while the head was small it was not out of proportion to the rest of the body. The bitemporal diameter was 11.5 cm., the biparietal 13 cm., the occipito-frontal 18 cm., occipito-mental 20.5 cm., trachelo-bregmatic 16.5 cm.; and the occipito-frontalis circumference 50 cm.

The autopsy revealed nothing macroscopically amiss in the brain or spinal cord. The weight of the brain after having been in formaline for about two weeks was 1,167 grams. The average weight of the normal brain being 1,230 to 1,350 grams, taking into

consideration the fact that the brain had been in formaline for 2 weeks, it could be estimated that the brain weighed considerably less than the average. The convolution of the brain showed no deviation from the normal.

Sections were made from the paracentral regions, from the pons medulla and from the cervical, thoracic, and lumbar regions of the cord.

The pia in the paracentral regions was thickened, and infiltrated with large mono-nuclear round cells, and connective tissue cells, the latter predominating. There was some peri-vascular distention and slight peri-vascular round cell infiltration in the superficial layers of the cortex in this region. The Betz cells were numerous and stained well, and the other cells of the cortex could not be said to be diminished in number or altered in their orientation.

No pathological change could be found in the white matter of the pons, medulla oblongata or spinal cord, either by the Weigert method or with the nuclear stain. The pyramidal bundles in the pons were perhaps a little smaller on the right side than on the left but otherwise no abnormality was noted.

The cells in the anterior horns of the spinal cord stained well and showed nothing abnormal except that in many there was a considerable amount of yellow pigment.

In a word there was no demonstrable pathological condition to account for the spastic diplegia dating probably from birth or at least early infancy.

CASE 3. B. J. About 10 years of age, died 2 days after a subcutaneous incision of the plantar fascia and Achilles tendon. The pathological diagnosis after autopsy was chronic mitral and bicuspid endocarditis, broncho-pneumonia, fatty degeneration of the kidney and liver. The patient was operated on at the University Hospital by Dr. Charles Frazier, having been transferred to this institution temporarily from the Vineland Training School.

The patient was a large plump boy with low mentality since birth. The facial expression was vacant, and he did not talk. Both arms were spastic, but he used the arms freely, grasping with each hand fairly well. It was impossible however to fully extend the elbow joint on either side. At rest the fingers of the right hand were extended. The bicipital jerks could not be elicited.

The lower limbs were somewhat smaller than normal from the knees down, and he was unable to stand. There was talipes-equinovarus on both sides, and also a marked contracture of the Achilles tendons. The ham-string tendons were slightly contracted. The patient was able to flex the hips well but could not extend them fully.

The brain was quite small, measuring in its long diameter but 6 inches. Twenty-seven brains at the neuropathological laboratory of the University of Pennsylvania were measured and it was found that the average length was a little over seven inches. No abnormality of the convolutions was observed and a cross section of the brain was apparently normal in appearance.

Sections were made from the right and left paracentral regions, the basal ganglia on one side, the optic nerves, the medulla oblongata, the cervical, thoracic and lumbar regions of the spinal cord and of the anterior roots from the cervical and lumbar regions, and these were stained by the Weigert method and by thionin and hemalum.

The paracentral regions. By the Weigert method no degeneration of the white matter could be demonstrated. There could be seen however in the superficial layer of the cortex a fine network of fibers and nuclei.

By the nuclear stain the pia was found to be thickened in places and especially over the sulci, where it was markedly so. The process consisted of an increase of connective tissue fibers which were studded with numerous connective tissue cells, some mono-nuclear round cells and some red blood corpuscles. In other places the pia was slightly thickened but was not the seat of any disease process. In the cortex of the paracentral region there was considerable peri-vascular dilatation but no infiltration of round cells in the peri-vascular spaces was found.

By the thionin stain, many of the Betz cells in the left paracentral region stained normally. Some however stained poorly and showed other signs of degeneration. Some of the cells were swollen, had lost their processes and the nucleus had disappeared. The Betz cells seemed to be present in normal quantities. Sections from the right paracentral region showed practically the same process except here and there degenerated Betz cells were more numerous.

The cells in the other layers of the cortex appeared to present no abnormality as to position and numbers on the right side.

The optic chiasm and the optic nerves took the stain normally. The basal ganglia showed microscopically nothing pathological.

Sections from the medulla oblongata and from the cervical and lumbar regions of the cord were entirely negative with the exception of some insignificant changes of the cells of the anterior horns in the thoracic region consisting of atrophy of the pigment and displacement of the nucleus.

There was some slight degeneration of the anterior roots in the lumbar region. The pia of the cord was not diseased and no cause could be found for the degeneration of the anterior roots.

The pyramidal tracts of the cord stained well and showed no evidence of degeneration.

In this case the degeneration of the Betz cells was hardly extensive enough to explain a condition which had existed since birth, and the process described was not one which suggested that it had existed for a long time.

No satisfactory explanation of the paralysis has been offered in the cases in which the pyramidal tract is apparently normal and in which insignificant or no lesion is found in the brain.

The part played by the pyramidal tract in these cases presents an interesting problem. Intact pyramidal tracts imply that they are capable of transmitting motor impulses and in those cases in which the pyramidal tracts are normal, a cause for the palsy must be searched for above the spinal cord or even above the medulla oblongata and the pons.

It is reasonable to suppose that the cells of the cortex may be at fault, and disease of the cortical cells may occur without causing degeneration of the pyramidal tracts. That this is true has been shown by Binswanger who cited a case of tumor situated in the central convolution, one of tumor of the dura, and one in which there was a focus of softening in the cortex, with intact pyramidal tracts.

Babinski also cited a case of tumor of the motor cortex with intact pyramidal tracts. He believed that the irritation of the pyramidal tracts was sufficient to cause paralysis, but not intense enough to give rise to secondary degeneration.

Finkelnberg advanced the theory that the cause of the paralysis in his case was to be found in the atrophy of certain cortical cells which presided over function, while the preservation of the large ganglion cells (*Riesenpyramidenzellen*) insured a trophic influence upon the pyramidal tracts.

A similar explanation may be applied to the case described by Spielmeyer under the name of intracortical hemiplegia, above cited.

Hoestermann's cases may be cited as supporting this theory also. He emphasizes the importance of a careful histological study of the cortex, especially in the central convolution. He believed that when by atrophy the large ganglion cells (*Riesen-*

pyramidenzellen) are isolated from other cortical cells they are unable to exercise a functional influence upon the pyramidal tracts but the intactness of the large ganglion cells guarantees a trophic influence upon these tracts.

Another explanation he finds in the fact that different parts of the brain develop independently and these later become associated with each other, and hand in hand the function becomes established. If a lesion occurs before the functional differentiation but after the conclusion of the anatomical differentiation the function is destroyed, and finally if the organ is completely developed and both functional and anatomical differentiation is completed there occurs both a functional and anatomical defect.

The role of the optic thalamus must be considered at least in some of the cases of infantile cerebral palsies.

Bischoff (32) believed that the symptoms of infantile cerebral palsy can be caused by disease of the optic thalamus, and that an implication of the pyramidal tracts is not essential. Bischoff has shown that destruction of motor functions may be caused by cutting off of the sensory stimulation from the optic thalamus to the motor cortex. The optic thalamus appears he claims to be associated functionally with certain zones of the cortex by means of projection fibers.

Recently S. A. K. Wilson has described cases of progressive symmetrical lenticular degeneration, presenting bilateral involuntary tremor of all the limbs, rhythmic usually, associated with spasticity of the limbs and face, dysarthria, dysphasia but little or no true paralysis. There is neuroglial proliferation, the glia replacing cells and fibers. There is also cavity formation and atrophy of the caudate nucleus. It is an extrapyramidal motor disease. Cirrhosis of the liver is a constant condition.

As the basal ganglia in my second case were normal it cannot be compared to this group of cases. Nor is there any resemblance to the cases of Oppenheim (33), which he described as pseudobulbar palsy occurring in children and exhibiting double athetosis, rhythmic tremor, associated movements without sensory disturbance or implication of the intelligence. Vogt (34) found in these cases a marble-like appearance together with atrophy of the caudate and lenticular nuclei.

In my own cases with the exception of the first case in which no Betz cells were found, no change in the cells of the cortex could be demonstrated. The explanations offered therefore by Finkelnberg, Hoestermann and Spielmeyer do not satisfactorily apply to these cases.

What the cause of the paralysis was in my cases is yet undetermined. Whether it be due to some deficiency of nerve cell which baffles our present methods of study to demonstrate; whether it be due to faulty connection between various layers of the cortical cells; whether the nerve fibers in the pyramidal tracts have not developed in sufficient numbers in the lower levels of the cord (Spiller); or whether the fineness of the fibers interferes with their perfect function by offering undue resistance to the transmission of the motor impulse from the cortex and thus preventing the full motor discharge to reach the periphery (Rhein), is still a matter for study in the future to determine. It is difficult to avoid the conviction that one must look, for the explanation of these cases, to some quality of nerve cell or fiber which cannot by our present methods be demonstrated.

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