

A CASE OF CHRONIC ADULT CHOREA, WITH PATHOLOGICAL CHANGES SIMILAR TO THOSE OF GENERAL PARESIS.

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THE subjoined case, offering a somewhat unusual combination of clinical symptoms, together with pathological changes in the central nervous organs very similar to the lesions noted in general paralysis of the insane, would seem to afford additional evidence of an intimate relationship between chronic progressive chorea and certain other neuro-degenerative diseases, notably general paresis.

A meagre family history only could be obtained. The patient, a white female, was of the lower class, a native of Alabama. Her father was insane, and had "some kind of nervous trouble" which, from the description given of it by one of his relatives, was probably chorea.

Patient from early life was looked upon as dull; she received no education; worked on a farm as a laborer. At the age of seventeen she married, and one year later gave birth to a child, having up to this time evinced no mental disorder which could properly be classed as insanity. She "never seemed the same" after her confinement, there dating from this time a change in disposition, a progressive increase in mental obtuseness, some irritability, a tendency to fits of anger, and some emotional weakness. At the same time peculiar jerky movements of muscles of the face and upper extremities were noticed. These choreiform movements, as well as the mental defects and perversion, grew more marked with the lapse of time; after two or three years, incoördinate movements in lower extremities appeared and gait became unsteady. The mental weakness finally became so pronounced that patient was adjudged insane and sent to the State hospital. Her general bodily health was reported to have been good.

Six years after the onset of the disease, an examination resulted as follows: Patient is a young woman, aged

¹ Read by title.

24, of large frame, and is well nourished, has a good color, makes no complaint of feeling ill in any way. She wears an expression of stupidity; forehead is low, teeth irregular, ears illshapen, with completely attached lobules; lungs normal; heart: a slightly roughened systole at apex; arteries not tortuous nor sclerosed. Urine: small amount of albumin, trace of indican, some hyaline and nucleated tube casts, with an occasional granular cast. Blood: hæmoglobin percentage, 90; number of red corpuscles in cubic millimetre, 5,920,000; temperature, pulse and respiration normal.

There are almost constant choreoid movements, chiefly affecting the muscles of the face, head, neck and upper extremities, resulting in twitching of the corners of the mouth, grimaces, spasmodic closure and opening of the eyes, twisting of head to one side, nervous, jerky, inco-ordinate movements of fingers and arms. There are also twitchings and choreoid spasm of muscles of the lower extremities, although these are, especially when patient is seated, much less noticeable than are the movements in arms and face. None of the movements are great in extent. All of them are more pronounced on left side than on the right. The tongue is protruded straight, but cannot be held out—is jerked suddenly back and teeth snapped together. The movements become more marked when patient is made aware that she is being noticed. They cease during sleep; are increased by voluntary movements. In addition to the choreic movements, there is a rhythmic coarse tremor of hands, well marked on left side, scarcely perceptible, though undoubtedly present, on right. At times, especially when she attempts to walk, or when her attention is concentrated on other matters, there are distinct, worm-like, athetoid movements in hands and fingers, these also best shown on left side. Patient is unable to execute any finer movements with fingers, and has difficulty in dressing and in taking her food. She swallows without trouble. When told to walk, she rises from her chair with difficulty, assisting with her hands as far as possible, sways, hesitates, executes a peculiar jumping up and down movement by rising upon her toes, starts forward, takes a few unsteady steps, stops suddenly, sways, rises on her toes two or three times, then goes forward again. Her steps are short and irregular, feet kept wide apart, she catches at the wall, pieces of furniture, or persons who stand near her. Her feet are raised high, heels put down first,

and often lifted two or three times before she gets her weight rested steadily upon the limb. Her arms are, when she is not allowed to grasp anything, held in a strained position, show choreoid movements, together with the slow athetoid twistings above mentioned. She cannot walk up or down steps. Sometimes falls to the floor. She stands fairly steady with eyes closed—about as well as with them open. Her muscular strength is much less than normal. Sensation, so far as may be judged from examination of one who is so demented, unimpaired.

Electrical reactions are entirely normal. Patella reflex, both sides, much exaggerated, more so on left; ankle clonus easily elicited, also most pronounced on left, where it will continue for several minutes. Triceps reflex increased, more marked on left side. Superficial reflexes normal. Pupillary reflexes normal. Ocular movements irregular and spasmodic; no nystagmus; spasmodic contractions in orbicularis palpebrarum marked. Vision: Slight myopia. Eye grounds normal under ophthalmoscopic examination, except for a small posterior staphyloma, both eyes. Speech irregular in tone and rhythm, gasping, articulation indistinct; difficult words are slurred, or no attempt is made to pronounce them.

Her mental condition is that of advanced dementia. She replies to most questions in monosyllables. Occasionally stares stupidly, wags her head and says nothing, even when the question is often repeated. Her memory is defective—she does not know her age nor the number of her children; is dull of comprehension, indifferent and careless, but not unclean in personal habits. Delusions cannot be elicited. She is irritable, petulant, easily angered. Is utterly unable to give any intelligible account of her own case, or to return reliable answers to questions asked her.

The condition of patient remained substantially as above described for three years, the only changes being gradual increase in dementia, in violence of choreic movements, and in the spastic symptoms. She was treated at different times with potassium iodide, arsenic, various tonics, and electricity, equally without good effect. The casts and albumin persisted in her urine, but at no time was there much œdema, nor any additional indication of renal inadequacy. Her general bodily state remained good until a few weeks before her death, which

occurred nine years after the onset of the chorea, from gangrene of the lung. During the last few days of her life temperature was high, and she suffered from acute diarrhoea. Age at time of death, 27.

Post-mortem examination, made three hours after death, resulted as follows:

Body.—Well nourished.

Heart.—Weight 8 ounces; small vegetations along edge of one cusp of mitral valve. Arteries: small athromatous patches in first inch of aorta, a small patch here and there in thoracic and abdominal aorta, and a considerable cluster of diseased areas at bifurcation of the abdominal aorta. Veins and small arteries not affected.

Lungs.—At the apex of left, a small cluster of cheesy nodules. In lower portion of upper lobe of right lung is a cavity two inches in diameter, having ragged, greenish walls, and emitting a characteristically gangrenous odor. The cavity is surrounded by a zone of consolidation, and the entire lung is well filled with blood.

Kidneys.—Both are firm, pale, capsule partially adherent, cortex pale, striæ indistinct, pyramids dark red, weight of right $3\frac{1}{4}$, of left $3\frac{1}{4}$ ounces.

The lower 18 inches of *ilium*, the cæcum, and the ascending colon, show signs of acute inflammation, the mucous membrane being thickened, red, injected, surface dotted with hæmorrhagic points. Other organs in abdomen and chest are normal.

The *skull* shows slight asymmetry; the bone is thick, diploë scanty, sutures open, inner surface pale. There is unusually firm adhesion to dura. Beyond this adhesion to calvarium, the *dura* shows no abnormality. The *pia arachnoid* is extremely thick, tough, œdematous, opalescent, and can, without difficulty, be removed in large sheets; it adheres to the convolutions here and there over vertex. The blood vessels are injected; the larger arteries show no atheroma nor other disease.

The *brain* weighs 38 ounces immediately after removal and with the pia attached. It does not fill the cavity of the cranium; is shrunken, and very firm, almost hard. All of the convolutions over the convexity are atrophied, and the sulci gape; the gray cortex is thinned, and its outer surface is in places irregular. The white substance is hard, puncta vasculosa few; the lateral ventricles are large, ependymal lining granular. The surface of the corpora striata and thalami, where visible in

lateral ventricles, is uneven and sclerotic to feel. The ependymal lining of fourth ventricle is granular. Cerebellum, pons and medulla abnormally firm and hard.

The *spinal cord* is firm; in the fresh specimen pathological changes are not pronounced, but after hardening in Müller's fluid a degeneration in pyramidal tracts becomes quite evident to the naked eye.

Portions of the fresh tissue from various regions of the cortex cerebri, and from pons, medulla and cervical cord were placed in absolute alcohol, cut and stained after the Nissl method, and by carmine. The remainder of the brain and cord was placed in Müller's fluid. Golgi silver preparations of the cortical tissue were subsequently made, and after several months in Müller, a silver phosphomolybdate stain, as recommended by Berkley, was attempted, but with indifferent success. After hardening in Müller was complete, portions of the cortex, basal ganglia, internal capsule, pons, medulla, cerebellum, and the several regions of the cord, were infiltrated with celloidin, cut and stained by the Weigert method, and by Pal's and Kultschitzky's modifications of the same; and sections also tinged by nuclear stains and by sodium sulphindigotate.

Microscopic study of the tissue resulted as follows:

In the *dura* no characteristic pathological changes were found.

Pia.—There is great thickening, most marked in degree over the convexity of brain, and reaching its height in motor and nearly adjacent areas; there is a general increase in connective tissue, and a marked round cell infiltration; there are accumulations of round cells near many of the blood vessels, and near the points at which pia adheres to subjacent convolutions. The adventitia of many of the blood vessels is thickened, and in a few of the medium-sized arteries, there is a thickening of muscular layer as well. At several points, small extravasations of blood are noted in meshes of pia. Most of the vessels are well filled. Over the cerebellum the changes in the pia are not marked, and also but slightly shown over basal portions of the brain.

Cerebral cortex.—The outer surface of the convolutions is in places uneven and irregularly indented, the first, or molecular layer, being of unequal thickness; the indentations correspond with points of adhesion to pia. The number of connective tissue cells in the first layer is increased. Among the nerve cells of the other layers

of the cortex extensive degenerative changes are noted, affecting alike the large and small pyramidal, fusiform and ambiguous cells. The most striking general change is an apparent *leanness*, a shrinking in size of the cells, pyramidal especially. In Nissl preparations there are noted disappearance of the normal rods and striæ of the large cells, increase in pigment deposits, irregularities of staining, some of the nuclei being deeply tinged, some of the cells diffusely stained. Many of the cell bodies are simple masses of large and small granules deeply stained. Some show vacuoles. A large proportion of the giant cells of Betz are shrunk, more or less distorted, and their characteristic chromatin rods are disintegrated into granular masses. Around many of the degenerating nerve cells accumulations of lymphoid or connective tissue cells are seen, here and there, a nerve cell being almost obscured by them. Groups of eight to fifteen cells around a small pyramidal cell are not uncommon.

In Golgi silver preparations many of the nerve cells show disintegrative changes and irregularities of contour of the cell body, irregular swellings and varicosities of the dendritic processes, with extensive denudation of the lateral gemmule. In silver, as well as in the Nissl preparations, the grouping of scavenger cells about the diseased nerve cells, is noted. Throughout all layers of the cortex there is an increase in the number of connective tissue cells. In silver preparations many of the glia cells show very thick, coarse processes, often in relation with a blood vessel or with diseased nerve cells.

The blood vessels of the cortex show thickening of their walls, adventitia in particular, but here and there involving the middle and inner coats as well; many are tortuous; looped; the perivascular spaces of all are enlarged, and aggregations of round cells within the perivascular space are common; round many of the vessels are pigmented masses—hæmatoidin granules. Some few of the vascular twigs seem normal.

The changes in the blood vessels and in the cortical cells are more pronounced in motor area than elsewhere; the diseased nerve cells are noticeably grouped together, and it is also noticeable that these groups of diseased nerve cells often lie adjacent to diseased blood vessels. As is usual, many of the nerve cells are of normal appearance, although in motor area a very considerable proportion present the changes above enumerated.

In Weigert preparations an average number of tangential fibres are stained; many of these show globose and fusiform swellings, with here and there some apparent disintegration of myelinic sheath. In the motor area there are among the radial fibres, many of the largest variety which show varicosities, fusiform swellings, with here and there the myelin broken up into coarse granules. These changes in the radial fibres are not noted in anything like the same degree in sections from posterior portions of the brain, and from the frontal convolutions, although in these localities occasional varicosities are seen. The simple varicosities are sufficiently frequent in normal nerve fibres, or are produced in manipulation, but the disintegration and marked irregularities in contour noted in some of the radial and tangential fibres of motor convolutions are undoubtedly of a pathological nature.

In the corpora striata and thalami, changes in the nerve cells are not well shown in sections colored with nuclear stains, and Weigert hæmatoxylin. There is the same seeming increase in the connective tissues noted in the cortex. Nissl preparations were not made. In Golgi silver preparations the glia cells stain in large numbers, and many show the thick processes attached to the blood vessels. In lenticular nucleus there are cells which show some abnormalities—irregularities and breaking down of cell body, with partial destruction of dendritic processes. There is nothing comparable with the degenerative change in cortex, however. The blood vessels in the basal ganglia show the same changes noted in cortex, but to a lesser degree.

The ependymal lining of the fourth and lateral ventricles shows numerous granule-like swellings, nearly homogeneous or containing a few nuclei, covered by the epithelial layer, which, over some of the little protuberances shows proliferation of its cells.

In the *cerebellum* comparatively few changes of a pathological nature are discovered by nuclear or Weigert stains. Silver preparations seem to show in the dendrons of many of the large cells, varicosities and disappearance of some of the gemmules, but as the preparations were of indifferent quality only, too much importance is not to be attached to the findings. The blood vessels are also for the most part comparatively normal.

In both pons and medulla there is some seeming increase in the connective tissue structures; the

blood vessels are tortuous, show dilated perivascular spaces with agglomeration of round cells therein. The cells of the nuclei of the cranial nerves are not markedly affected, save those of the nucleus of the twelfth, in which there are noted a decided increase in fatty pigment, with granular disintegration in some cells.

In Weigert preparations many degenerated nerve fibres are discoverable in the pyramidal tracts of both sides, more noticeable in medulla, but readily distinguished in pons and in crura cerebri.

Spinal cord.—The pia is but little altered. Its blood vessels show adventitial thickening. Within the cord the connective tissue trabeculæ seem increased in number and thickness, and connective tissue nuclei are numerous.

The nerve cells of the cord are of fairly normal character.

The chiefest and most striking pathological change is degeneration in the pyramidal tracts, both crossed and direct, throughout their extent, well marked on both sides, but somewhat more pronounced on the left in crossed columns. It is estimated that one-third of the fibres at least are destroyed. There are also evidences of degeneration in other portions of the cord, noticeable in the tract of Gowers, where the destruction of nerve fibres is quite considerable. In the anterior root zone, especially its peripheral portions, diseased fibres are noted. The columns of Goll and Burdach seem of normal structure. Sections of the peripheral nerves were not made. Their roots, as seen in sections of the cord, are normal.

Clinical summary.—Chorea, developing at the age of 18, following child-birth, associated with progressive dementia, athetoid movements of upper extremities and spastic paralysis. Death from gangrene of the lungs at the age of 27. Pathological changes: Thickening of pia; disease of the blood vessels of pia, cortex and other portions of the brain; extensive degenerative changes in cortical nerve cells, especially in motor region, and degeneration of pyramidal tracts throughout their extent, with slight degenerative changes in fibres of other portions of the cord.