The Journal OF Nervous and Mental Disease

An American Journal of Neurology and Psychiatry, Founded in 1874

Original Articles

A LESION IN THE PUTAMEN

BY L. NEWMARK

SAN FRANCISCO

In the right putamen of an aged man, with intense sclerosis of the arteries of the brain and cord, a condition was observed which, it is thought, may be interesting because it at least closely resembles, if it is not identical with, that which has been described in the youthful victims of progressive lenticular degeneration.

History of the Case.—In September, 1911, a man, aged 65 years, was sent by his doctor, who wrote that the patient had a tremor in his left hand, and that the left side was affected in a manner which suggested the diagnosis of "onset of Parkinson's disease"; the condition had been "coming on this past year," during three months of which the patient had been under the observation of the writer of the letter; and advice was asked regarding treatment which might "prevent the other side from being involved."

The patient himself related that about a year and a half before, he had fallen sick with stomach trouble and had lost weight, but was now better; he was still weak, however. The inefficiency of his left arm was first noticed while shuffling cards one day in the summer of 1910. It had happened on one or two other occasions that he could not articulate, although he knew what he wanted to say. Within the last few months he had noticed a "numbness" in the left arm, and later a tremor; he could not perform habitual movements with the left hand as well as before, and could not move the left toes as well as the right. The left leg was not as strong as the right, but he had

observed no tremor in it. When he shut the left eye, however, he felt a tremor which did not occur when he shut the right. In his youth he had had gonorrhea, and, he thought, "one or two chancres."

There was at first sight nothing striking in the aspect of the man or in his movements or in his mode of speaking. Neither myself nor certain others who observed him with me shared the impression of incipient paralysis agitans. This impression had evidently been caused by an appearance of slight stiffness and clumsiness in the left hand, which was discolored to a reddish hue, and by the tremor. The attitude of the hand was not, however, that of paralysis agitans, and the tremor was not present when the hand was not voluntarily moved. During voluntary movement there was a fine regular tremor, of no considerable severity, quite like an ordinary mild senile tremor. There was no complaint about the right hand; in it only a very slight trembling could be detected when the arm was extended; it was hardly pathological in degree.

Extension and flexion of the left elbow were performed with slightly less power than would have seemed normal. The grip of the left hand was distinctly diminished. In the left lower extremity there was also a slight loss of power: the toes could not be wriggled with quite the same ease as those of the right foot, and flexion of the knee, and dorsiflexion of the ankle were executed with less strength than on the right side. But all other motions were quite forcible.

There was no difference in the radius or elbow reflexes, knee-jerks, heel-jerks, or plantar reflexes, between the two sides. All of these were perfectly normal. Concerning the abdominal and cremaster reflexes there is unfortunately no note.

Sensibility in all its modes was normal throughout; there was no astereognosis, no ataxia, the sense of passive movements and that of posture in the fingers of the left hand was keen. In putting the left forefinger to the nose the patient would remark that this was not done with the same ease as with the other hand, though no difficulty was apparent to the observer. The pupils, optic discs and all the other cranial nerves were unaffected. There were cardiac murmurs, referable to the mitral and aortic valves. The Wassermann reaction in the blood was negative.

Observation of this case was interrupted by intervals of months. In May, 1912, the patient mentioned that he had been wetting the bed of late. It was discovered that there was a large amount of residual urine, in consequence of a paresis of the bladder. The man was instructed in the use of the soft catheter. He reported the next

day that the urine was bloody; but he was suffering no pain. Cystoscopic examination by a specialist disclosed an area in which the bleeding had taken place. A week later there was no visible evidence of the hemorrhage, and none recurred. There was no hypertrophy of the prostate. The vesical weakness had been followed soon by fecal incontinence. Power over the anal sphincter returned to a considerable extent, but the patient was dependent upon the catheter for the rest of his life.

At this time (May, 1912) the spinal fluid was examined. The Wassermann, Nonne and butyric acid tests gave negative results. Fehling's solution was not reduced. The cells averaged five per cubic mm.; all were lymphocytes. The report added that the fluid contained a shreddy precipitate, which increased on standing.

Through an oversight the patient was allowed to depart without a blood count having been made. The omission was vexatious, and we sought to communicate with him, and with the doctor who had sent him, in order to obtain the information wanted; but without success. Our belated zeal, however, was not inspired by any suspicion of an abnormal state of the blood. Accordingly, the result of a blood count made immediately after his reappearance in January, 1913, was surprising: there were 600,000 white and 4,750,000 red blood corpuscles, and the Hb was 95 per cent. Of the white corpuscles 90 per cent. were lymphocytes, 5 per cent. large mononuclear and 5 per cent. polymorphonuclear. On another occasion 700,000 white corpuscles were counted. The patient was considered to be afflicted with lymphatic leukemia.

Meanwhile nothing else had changed. The condition of the left extremities was as before. Neither spleen nor liver was enlarged, nor were the lymph glands.

Dr. W. F. Beerman, who attended the patient during the last year of the man's life, states that there was a progressive debility, with occasional delirium; sometimes the confusion passed off in a few minutes, at other times it lasted several hours, towards the end it continued for several days. There was no other change whatever in the neurological condition from that which has been described. Death occurred February 14, 1914, about three years and a half after the trouble in the left hand was first noticed.

Anatomical Examination.—Dr. Beerman performed the autopsy under very inconvenient circumstances; what he brought away was preserved in formaldehyde. It was about two years later that I first inspected the material, and found the brain, which was uncut, the spinal cord, of which the lower end and most of the cervical part was

missing, the spleen, a kidney, a small piece of the liver, and a bit of a rib. No enlarged glands had been seen at the autopsy. The pia mater, it is said, appeared in the fresh state as if there had been a severe purulent meningitis, an impression caused by the leukemic condition.

The spleen, after the long immersion, was not larger than a normal organ. In it, as well as in the kidney, the rib and the liver there was found on microscopic examination an intense lymphocytic infiltration. In view of the concurrence which has been described of

FIG. 1. Coronal section passing through optic nerves. Right putamen slightly smaller than left.

remarkable changes in the liver with disease of the lenticular nucleus it should be emphasized, perhaps, that no other affection was found in the piece of liver than the foci of lymphocytes.

The pia mater could be stripped from the brain without difficulty. A section through the brain in the coronal plane, passing through the lenticular nuclei, disclosed a marked difference in size between them, the right appearing much shrunken.

Large blocks of tissue were kept in bichromate of potassium for several months; this necessitated dependence chiefly on Weigert's

stain for myelin and on the Van Gieson mixture in preparing that part of the material for examination with the microscope.

Microscopical Examination.—There is a general arterio-sclerosis throughout the meninges, of long standing and of high degree, dense fibrous thickening of the coats causing narrowing of the lumen, in some of the vessels almost to their total occlusion.

FIG. 2. Section through anterior part of globus pallidus and optic chiasm.

There is a very abundant infiltration of the pia mater with lymphocytes, throughout the length of the cord and about the brain, the congregations of cells being more numerous at the base of the brain than over the convexity, and, in the spinal region at least, around the veins than around the arteries. Occasionally an accumulation of lymphocytes is seen about a vessel within the nerve-roots. The infiltration with the small round cells permeates in many places all the layers of the pia mater, but the substances of the cord or brain appears to be invaded relatively only very slightly, scattered lymphocytes being found here and there in the marginal glia. One gets the impression that the pia has acted as a filter, allowing a comparatively insignificant number of corpuscles to pass through. Where larger foci of round cells are seen an extension of the connective tissue of the pia can generally be traced. The villi of the choroid plexus, the

pineal gland, and the substance of the only intervertebral ganglion which was examined, were also found to have been spared the leukemic infiltration.

The condition revealed by coronal sections through both hemispheres, stained by a modification of Weigert's method, is illustrated by the series of photographs, which were supplied with great liberality by Dr. H. D'Arcy Power. In Figs. 1 to 4 a difference in size between the two hemispheres is discerned. It becomes grad-

FIG. 3. Diminution of putamen and globus pallidus at level of anterior commissure.

ually clearer, as we proceed from the first to the fourth section that there is a shrinking of the right putamen. At first, a difference in the supply of myelinated fibers in the putamen is not discerned; it is the Van Gieson stain which shows under the microscope the changes in the anterior planes represented in the series. Before the globus pallidus appears, proliferation of neuroglia is detected first in a small area in the lateral part of the putamen, near the external capsule, about midway between the dorsal and the ventral extremity of the putamen. This neuroglia proliferation spreads gradually in a mesial and in a vertical direction as the sections proceed caudalwards. At the level of the median part of the anterior commissure

(Fig. 3) the proliferated neuroglia is still confined to the lateral region of the putamen, where the myelin stain shows the presence of fibers running more or less vertically; some of these are degenerating. The pathological process denoted by the increase of neuroglia has at this level hardly invaded the region of the fibers which radiate towards the globus pallidus, but soon (Fig. 4), before the mesial medullary lamina of the globus pallidus becomes well developed and enables an inner zone of the globus to be distinguished, it becomes evident that the nerve pencils passing towards the lateral

FIG. 4. Shrinking of right putamen and diminution of right globus, but other gross changes in central ganglia not visible.

lamina are not as large as those in the other hemispheres, the finer, pale fibers becoming deficient. The diminution of these fibers can dorso-ventrally; but in the dorsal corner of the globus, in the angle included between the lateral lamina and the internal capsule, the pale, fine, yellowish fibers, which pass between globus and caudate nucleus, are abundant. At this level the proliferated neuroglia occupies an area extending about two thirds of the way across the putamen from the external capsule; dorsally it has slightly encroached upon some of the bridges of gray matter between the fibers of the internal cap-

be traced into the globus pallidus at about its middle third, reckoning sulci, and ventrally it has extended not quite to the base of the putamen. Thus far the naked eye perceives in the Weigert sections in the lenticular nucleus nothing more than the shrinking of the putamen, the contraction of which has been almost exclusively in its width, and the slightly smaller size of the right globus pallidus. Radial bundles of fibers can be seen directed towards the external lamina, and the substance of the putamen has not undergone gross changes.

FIG. 5. Cavitation in right putamen.

But about the level of the genu of the internal capsule, at the anterior extremity of the optic thalamus, where the globus pallidus has two distinct zones, and where the lenticular ansa appears (Figs. 5 and 6), the pathological process in the putamen becomes more intense. Not only are the perivascular spaces larger than hitherto, but large spaces have formed through almost the whole vertical extent of the putamen, in consequence of the breaking down, or tearing, of the neuroglia, and of the opening of the spaces thus formed into the large ones around the blood vessels. Around a vessel at the base of the putamen there is a large mass of lymphocytes, but within the putamen itself lymphocytes do not appear in considerable numbers

which might indicate a special affection of this region by the leukemia. The vessels within the affected area are not conspicuously diseased, although some "lacunes" are observed around them; some vessels appear even rather thin-walled. The neuroglia is very rich in nuclei, which, retaining some of the stain after differentiation by the method of Pal, give to the ground substance in the Weigert sections a granular appearance under a lower power; by this appearance the presence of the disease in the putamen may often be detected before the

FIG. 6. About same level as in Fig. 6, enlarged. Cavitation. Abundant fibers in lenticular ansa.

loss of myelinated fibers becomes clear. Another indication of the morbid process in Weigert sections is the presence of pigment granules. This pigment is not observed in the left putamen.

Before the appearance of the ansa, as in Fig. 6, there are still a number of fiber bundles in the putamen which contain the paler, finer fibers as well as darker ones; but after this the degeneration of the fibers becomes more extensive and more intense, the finer fibers seeming to disappear first, for what is left of a bundle is always composed of thicker, darkly-stained fibers.

FIG. 7. Section through anterior end of thalamus. Atrophy and degeneration of putamen. Anterior part of Forel's lenticular bundle normal.

The corrosion, or moth-eaten look, of the putamen is striking; but in a carmine or Van Gieson section the disease stands out distinctly even where there is no cavitation. In a large section viewed under a low power the proliferated neuroglia quickly catches the eye.

In the plane of the genu of the internal capsule, where the morbid process has reached its highest degree, there is still a very slight difference in size between the globi pallidi of the two hemispheres, but soon, in the plane passing through the middle of the mamillary tubercles (Fig. 7) it becomes doubtful whether there is still this inequality. The lateral lamina appears thinner on the affected side, chiefly on account of the loss of fibers passing to it from the putamen. Within the lateral zone of the globus the characteristic fibers from the putamen are conspicuously absent; those of similar appearance in the dorsal region of this zone, which pass between the globus and the caudate nucleus through the internal capsule, are as abundant as on the left side. There is a dense network of darkly-stained fibers of varying caliber in each of the two segments of the globus; but one gets the impression that there is a still greater wealth of thick, dark, transverse fibers in the left globus than in the right, even in the mesial segment. Towards the ventral part of the globus, however, there is no visible difference in the supply of myelinated fibers between the mesial segment in the right and that in the left half of the brain. The ansa, ventral to the globus (Figs. 6 and 7), is as well developed on the affected side as on the other, and this is likewise true of the fibers which issue at the dorsal part of the periphery of the mesial zone and pass tangentially to it mesialwards, towards the anterior thalamus (Fig. 6).

The disease in the lenticular nucleus is still intense in the region exhibited in Fig. 9 (the figure is *reversed*). The neuroglia is still breaking down in the lateral part of the putamen in the middle third of its dorso-ventral dimension, and its overgrowth extends here through the whole width of the putamen, approaching close to the globus pallidus. Further caudalwards the tissue ceases to present the moth-eaten aspect. The ventralmost part of the putamen, which turns off laterally at an angle, is normal throughout, even where an increase of neuroglia is observed in all the rest of the putamen. The loss of myelinated fibers in the posterior part of the putamen and in the remnant of the adjoining globus pallidus is manifest (Fig. 10). Thinning and pallor of the external capsule are also noticeable.

Even after the putamen has been split up into islets by retrolenticular fibers, at the level of the external geniculate ganglia, an increase of the glia nuclei continues to distinguish the right putamen from the left, although there is a great lessening in the intensity of the affection.

It should be stated that in the *left* putamen in various planes areas of increased glial nuclei are now and then to be found. In its

caudal portion, at about the level shown in Fig. 10, this increase of glial nuclei is quite diffuse, except in the ventral region.

The projection system of the globus pallidus appears to be normal (Figs. 7 to 10). In Fig. 9, which furnishes a magnified view of the structures exhibited in Fig. 8, Forel's lenticular bundle appears larger on the side of the lesion than on the normal side, while the corpus subthalamicum of Luys is smaller on the former. This is due to a slight obliquity of the sections, the effect of which is still

FIG. 8. Section through posterior limb of internal capsule and cerebral peduncles.

more pronounced in Fig. 10. The normal side is cut further caudward than the affected side. The right internal capsule, regarded by itself in the successive planes of the series, shows no degeneration. When viewed in comparison with the other, however, a difference is observed between the two sides at the levels represented in Figs. 8, 9 and 10. The right centrum semiovalis appears smaller, the right internal capsule is not quite so broad as the left, and particularly the fibers which descend from the lateral part of the foot of the corona radiata and cut the dorsal corner of the putamen to pass along the lateral edge of the internal capsule, are not so massive on the right side as on the left. The difference between the two internal capsules which is to be seen in Fig. 10 is caused by the obliquity of the section.

In the cerebral peduncles (Figs. 8, 9, 10) and in sections at subsequent levels showing the peduncular bundles descending in the pons, no difference is noted between the two sides either in Weigert or in Van Gieson specimens. The retrolenticular internal capsule appears quite normal; so do the superior cerebellar peduncles.

FIG. 9. Part of Fig. 8 enlarged. The picture is *reversed*. Atrophy and degeneration of right putamen; loss of fibers in globus pallidus. Forel's field, Forel's lenticular bundle, cerebral peduncle appear normal. Right internal capsule slightly diminished.

Material from the lowest part of the pons and the upper medulla oblongata was lost, for the most part. A Weigert section passing through the region of the acoustic nerve and cutting the pyramids above the olivary bodies shows a pallor at the ventral tip of one of the pyramids (the side was not marked here), and in another section, likewise unmarked, lower down and involving the olivary bodies, there is an area of altered myelin, extending from the ventral edge of one of the pyramids, just lateral of the arcuate nucleus, a little way dorsalward. Madame Vogt¹ gives photographs of similar pallid areas in this part of the pyramids in her paper on *État Marbré du Corps Strié*; in her case these patches were apparently bilateral, and she gives good reasons for supposing them to be artefacts, noting especially the absence of reaction in the glia. An increase of neuroglia in this case is of the slightest, if it really exists at all.

¹ C. Vogt. *Journal für Neurologie und Psychologie*. Vol. 18, 1912. Plate 43.

Whatever the nature of these patches of altered myelin may be, farther down the *right* pyramid is distinctly, though very slightly, affected in a manner which is likely to have pathological significance (Fig. 11). In sections in which the myelin sheath is stained it is always slightly, but indubitably, lighter than the other pyramid, the degree of difference being about the same in densely stained preparations and in those in which the differentiation has been carried farther or in which the hematoxylin lake was originally less dense; and this may be observed in specimens from various blocks all the

FIG. 10. Section through red nucleus, peduncles and anterior part of pons; section is oblique. Pale areas in centrum semiovale due to insufficient chrome. Degeneration of right putamen and external capsule.

way down to, and through, the motor decussation, and at the lower end of the decussation the lighter stain may be detected in the left crossed pyramidal tract. The difference between the two pyramids is still less marked in sections stained with carmine or with the mixture of picric acid and fuchsin; a keen-eyed pathologist, to whom such a section was submitted, declared himself at first unable to discern the difference, although he had found the evidence of the Weigert stain clear enough. Yet there is an extremely slight increase in the neuroglia in the right pyramid. Most of the cervical cord was either not obtained or was greatly damaged. Sections from its lower

part and from the upper part of the dorsal cord show in the area of the right uncrossed pyramidal tract a loss of myelin and what appears on close comparison with the tissue on the other side to be an extremely slight increase of glia, not detectable otherwise; while in the postero-lateral column on the left the pyramidal area is not at all distinguishable in Weigert sections, but here again comparison with the other side seems to disclose an increase in the neuroglia.

FIG. 11. The paler pyramid is the right.

Below the upper dorsal region no pyramidal affection could be made out.

The manner in which the brain was prepared not having been favorable to the study of cell changes, it only remains to say that such specimens as were obtained indicated that the cells of the putamen could hardly have survived in considerable number, or preserved their function, where the glial proliferation was abundant. The process which originated in the putamen and lead to the changes shown in the illustrations does not seem to have encroached upon the globus pallidus to any marked extent, the loss of myelinated fibers in the latter appearing to be secondary to the affection of the putamen. Accordingly, nerve cells are observed to be present in the globus; whether they have undergone considerable diminution in

number or finer structural changes could not be satisfactorily determined. Near the caudal end of the globus the tissue is rarefied around the blood vessels. The large cells are numerous in the basal ganglia of Meynert on both sides.

SUMMARY

The gist of the foregoing is that a man, advanced in years, after having experienced a transient disturbance of articulation some time before, suffered a slight impairment in the use of the left extremities, which appeared to him as a "numbness" or awkwardness in the action of the left hand, and a loss of facility in moving the left toes, and was associated with a slight tremor of the left hand on voluntary movement, and of the lid when he shut the left eye. By his first medical attendant the disease was considered, after an observation of three months, to be progressive and, possibly, incipient paralysis agitans. In the remaining two years and a half of the patient's life no further progress in the affection of the extremities was observed; but about a year and a half before his death paralysis of the bladder and weakness of the anal sphincter supervened. There was no Babinski sign of involvement of the pyramidal tracts, and all the tendon reflexes were normal, but the record contains no mention of the abdominal or the cremaster reflex. Subsequently lymphatic leukemia was detected, probably not until it had existed a considerable time, and of this disease the patient died.

Anatomically, leukemic infiltration is found in various organs and in the meninges of the brain and the cord; the arteries supplying the central nervous system are profoundly sclerosed; in the lenticular nucleus of the right hemisphere the putamen is shrunken, its contraction being almost exclusively in the lateral dimension, many of its nerve fibers are degenerated, and its area occupied by a mass of neuroglia with abundant nuclei, the changes taking place in this neuroglia leading to an appearance of corrosion or cavitation of the putamen, while the putamen of the other hemisphere shows only comparatively slight proliferation of the glia nuclei. The caudate nucleus of either side is unaffected. The right globus pallidus is hardly more than secondarily involved, through the loss of fibers which pass between the putamen and it. The myelinated fibers of the striothalamic and striohypothalamic systems have suffered no appreciable diminution. Finally, a slight degeneration in the right pyramid appears in the medulla oblongata and is traced faintly into the upper dorsal cord.

The lesion in the putamen resembles in so many particulars what Wilson² has described in his well-known paper on progressive lenticular degeneration that his words might have been transferred and found quite apposite to the condition before us; this applies even to the blood vessels for the most part, their relative thinness, for instance, despite the intense sclerosis of the arteries so widely prevailing.

One will not be easily dissuaded from associating this degeneration and shrinking of the putamen somehow with the arterial disease in this case, and may assume that there is here from this cause an effect which elsewhere may arise from other causes. Such cases as van Woerkom's,³ however, must be borne in mind, where, in a man of 65 years, there was advanced atrophy in the central ganglia with degeneration of nerve fibers and proliferation of neuroglia, yet the blood vessels were considered to be in very good condition for a person at that time of life. Even for the "lacunes" of the aged, with their sclerotic vessels, Marie,⁴ who found them most frequently situated in the putamen, is impelled to inquire, in view of the pronounced dilatation of the perivascular spaces, whether it may not be a sort of "vaginalite destructive" that affects the tissue as if by a progressive corrosion: the sclerosis of the vessels did not seem to suffice by itself, for in the area of the morbid change the vessels were quite pervious and contained blood corpuscles. Whether it be arterio-sclerosis or "destructive vaginalitis," the anatomical effect in the case before us presents a striking likeness to that which is so regularly observed under the very different conditions of Wilson's disease. Unfortunately nothing is known concerning the time of onset of the leukemia, so that it would be vain to speculate regarding an influence possibly exerted by that disease upon the putamen.

The paralysis of the bladder and the rectum may have been caused by a leukemic focus in the lower part of the sacral cord, which could not be examined anatomically; but if the leukemia had involved the spinal pia at the time the paralysis occurred, it is surprising that the spinal fluid contained so small a number of lymphocytes. The painlessness of the lesion which caused the hemorrhage of the bladder and the insensibility to the large amount of residual urine would seem to indicate that the origin of this paralysis was rather in the cord than in the corpus striatum, to demonstrate the in-

² S. A. K. Wilson. *Brain*, Vol. 34, 1912, p. 295.

³ Van Woerkom. *Troubles des Mouvements actifs dans la Lésion du Corps Strié. Nouvelle Iconographie de la Salpêtrière*, Vol. 27, 1914-15, p. 273.

⁴ P. Marie. *Des Foyers Lacunaires de Désintégration*, *Revue de Médecine*, 1901, XXI, p. 281.

fluence of which upon the bladder a number of observations have been published.

As for the tremor and the very slight hemiparesis, constituting a clinical picture which suggested paralysis agitans to at least one mind, support may be found therein for Wilson's theory of a "steadying effect" exercised by the corpus striatum on the action of the cortico-spinal system, the slightness of the syndrome being conceived as due to the integrity of the projection system of the globus pallidus, while the actual symptoms may be ascribed to the partial withdrawal of some influence which the putamen normally exercises upon the globus pallidus through the internuncial fibers, in this instance found to be degenerated to a considerable extent. Whatever this influence may be, one may suppose it, on anatomical grounds, to have been partially maintained by fibers passing from the caudate nucleus to the globus pallidus. Objections to this reasoning may be based on negative clinical observations and on the negative results of experiments on animals, the latter having been supplied by Wilson⁵ himself. Those who hold with the late Professor Dejerine⁶ that nowadays the lenticular nucleus is tending to become a sort of "caput mortuum," in which the attempt is made to localize the lesions of different affections with a more or less variable symptomatology, have here a slight, and rather obscure, affection of the cortico-spinal tract with which they may account for these symptoms.

⁵ S. A. K. Wilson. *Anatomy and Physiology of the Corpus Striatum*. Brain, Vol. 36, 1914.

⁶ J. Dejerine. Discussion in *Revue Neurologique*, 1914, Vol. 27, p. 726.