THE JOURNAL OF NEUROLOGY AND PSYCHOPATHOLOGY

SEP 6 1932

Vol. XIII.

JULY, 1932.

No. 49.

Original Papers.

HÆMORRHAGIC AFFECTION OF CORTICO-NEOSTRIATAL SITE REVEALED CLINICALLY BY ACUTE AND FATAL CHOREA.

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THE pathogenic problem of choreic and athetotic syndromes is far from being finished. A strictly striatal origin seems to be rendered doubtful on both theoretical and factual grounds; and it is the meritorious work of S. A. K. Wilson that has replaced the study of this complex type of involuntary movement on a physiological basis.

As a result of his researches, Wilson assigns to choreo-athetosis the validity of a syndrome connected not with unchanging lesions of a fixed apparatus but due to involvement of a system in which the cerebral cortex is one of the nodal points. This conception permits the integration, in one physiopathological totality, of choreo-athetoses from lesions of the cerebellar peduncles, of the thalamostriatal apparatus, and finally from those accompanying frontoparietal lesions to which he has given special attention. Wilson's hypothesis has been accepted by some writers and rejected by others. It is open to discussion not solely in respect of its anatomical basis; nevertheless every careful clinicoanatomical observation deserves to be documented and pondered over. The following observation furnishes support to the views of Wilson because of the extent of the frontoparietal lesions contrasted with the preservation of the cerebellothalamic system. It is not, however, a pure case; the involvement of the neostriatum is of importance. The extreme acuity of the case, which evolved in 36 hours and culminated in death, confers on it an exceptional clinical character.

PERSONAL CASE.

Rah . . . , male, age 28, cabinetmaker, enjoyed normal health to the age of 20. During his term of military service he contracted an acute and serious

polyarthritis, complicated by a systolic murmur at the apex. The affection seemed to disappear spontaneously, and from 21 to 25 he appeared healthy enough. A relapse occurred in 1927, the joints of the legs, especially the ankles, being concerned. He lay in bed for three months, then resumed his trade.

On February 16, 1930, at home after work, he felt violent pains in his head and was nauseated and fatigued. His tongue was coated. The headache was localized mainly above the eyes and over the forehead; a degree of photophobia was experienced. All the limbs ached, but no paralysis was present. Pulse-rate 110; temp. 38.6° C.

During the night his brother found him groaning, rolling about the bed, muttering unintelligible words, the prey to unceasing agitation, and recognising no one. By way of answer to questions he put his hands to his forehead. He kept beating his head against the bed, threw himself about, and knocked his left arm against the wall till it was covered with bruises. There was no complaint of diplopia; involuntary micturition occurred. At 3 a.m. the temperature was 39.1°. The motor agitation became ever more violent, necessitating his removal to hospital at about 4 a.m. On admission his temperature was 40.2°, his pulse 110; respiration was quick and shallow.

He was seen by us on the morning of February 17. Thin, and covered with ecchymoses, he was in the grip of clown-like movements recalling certain theatrical attitudes of hysteria but more abrupt and rapid than we have ever seen. From the time of his admission two attendants had been watching him and holding him down, for the movements were violent enough to toss him on to the floor. Mattresses were arranged against the wall to diminish the risk of injury. His face was flushed, his eyeballs turned up at intervals, his glance changing so that it was impossible to catch his eye. It was doubtful if he recognised us. The head was seized with movements of hyperextension as he lay on the bed, accompanied by extension of the trunk in an arc de cercle, while the arms were raised. From time to time clamping and opening movements of the jaws occurred, and movements of swallowing, accompanied by grimaces like those of athetosis. He made no cries, emitting only raucous guttural sounds. Occasionally a little blood trickled on the lips, from biting of the tongue or friction movements. The opisthotonic contractions were often lateral, the opposite leg crossing in semiflexion the leg of the side to which he was turning. During this time the arms were elevated violently, fingers extended, forearms in hyperpronation; such movements were nearly always bilateral and more or less symmetrical. The posture would be maintained for several minutes, then the muscles would relax, the limbs would sink to the bed; and after repose of some minutes another series would commence. In the lower limbs, the movements often consisted of uni- or bilateral extension with adduction, eversion of the feet, and extension of the great toes. The abdomen would retract, and it was not rare to observe the bladder empty itself spontaneously. Apart from the big movements of the upper limbs, held in the air like the sails of a windmill, grasping movements of the hands also were noted, and appeared to be voluntary. Objects seized in the hands were held with persistence. Occasionally, one of the arms came alongside the body and rotated inwards. The diaphragm took part in some movement-complexes. At other times the limbs were at rest while trunk and shoulders were the seat of bizarre contortions recalling the movements of Huntington's chorea.

Dominating the whole clinical picture were the amplitude, range, and violence of the movements, their asynchronicity, arrhythmia, and tendency to become generalized.

Examination was difficult because the patient violently withdrew any limb that was touched. This action set free a whole series of coarse movements necessitating his being immediately held to prevent his falling. Liquid was refused; sometimes he could be made to swallow a mouthful, but he choked and coughed, without return through the nostrils. He tried to bite those who were helping him to drink. The neck was stiff, but it could be rather easily made to relax, and there was no rigidity comparable to that of meningitis. Put on his feet, the patient was thrown down by the increasing violence of the movements. He could nevertheless maintain the erect posture, but the effort was interrupted by sudden loss of control of the limbs, and down he would go again. Walking was dominated by such involuntary acts.

The plantar reflex was indifferent on the two sides; the abdominals could not be tested. The pupils reacted to light. Tendon reflexes appeared feeble but were difficult to examine.

In the presence of this clinical syndrome we naturally thought of a superacute chorea whose violence we had never seen equalled even in the encephalitis of pregnant women. The motor disorder however was very different from that of Sydenham's chorea, in which the movements are more limited, milder, more selective and less brutal than in our case. Careful enquiry elicited no toxic cause. Blood urea and nitrogen turned out to be normal. Blood-sugar was down a little (0.71); in the urine was neither acetone, sugar, nor albumen, and no casts. The blood count gave 9,700 whites, with a lymphocytosis of 46 per cent. Blood cultures were made by Dr. Wittebroodt. A lumbar puncture could not be thought of unless under an anæsthetic. We were surprised at the rapidity with which quiet developed. Six minutes after the commencement of the anæsthesia the clown-like movements had all disappeared, leaving only the diaphragmatic contractions, the extensor movements of the legs and those of jaws and neck. These too vanished as the sleep became deeper. Babinski's sign was never present. By lumbar puncture performed with care at three different levels a hæmorrhagic fluid was got in all three tubes. It proved to be free of organisms.

Narcosis was prolonged in order to inject 500 c.c. physiological saline, and awakening was extremely slow. The motor disturbances returned in a certain order. First came the movements of mastication, protrusion of tongue, torsion movements of the neck, elevation of one shoulder, then more violent spasms of extension and elevation of the limbs. Only after two hours did all come back as before the anæsthesia, yet were less violent. Towards evening the patient was less agitated, but remained unconscious. The tendon reflexes were abolished in all four limbs, without Babinski's sign. During the night he became comatose and died towards morning.

To summarize: a young man who had had several attacks of acute polyarthritis, but none for three years, suddenly developed a superacute chorea terminating fatally in 36 hours.

The illness commenced with fever. It was not uræmic. Examination of different viscera revealed no trace of exogenous poison. Blood cultures were negative. In view of the antecedents an acute rheumatic encephalitis might be postulated, but only these antecedents could be adduced in favour of the speculation.

PATHOLOGICAL EXAMINATION.

The autopsy was made 18 hours after death, the brain having been hardened by formalin in situ. Lungs, intestines, heart and liver were normal. The spleen was twice the normal size and very friable. The

FIG. 1. Macroscopic appearance of the brain.

kidneys showed signs of degeneration and the capsule was more adherent than usual. Some myocardial degeneration was found, with petechial spots on the left side of the intraventricular septum. The valves were all normal, as were aorta and coronaries.

Macroscopic appearances.—The anterior two-thirds of the cerebral hemispheres were covered by a kind of hæmorrhagic sheet (without lesion or fracture of the cranium). This hæmorrhagic meningeal infiltration was most pronounced over the frontal poles and the rolandic areas (fig. 1). It was also well marked over the ascending parietal gyri, the superior parietal

and the supramarginal. It was much less intense over temporal and occipital regions. On the base, a vast hæmorrhagic sheet extended across the interpedunculo-chiasmatic space and insinuated itself past the hippocampus to the corpus callosum and anteriorly into the interhemispheric fissure. A series of vertico-transverse sections showed that the hæmorrhagic lesions of the brain were confined almost exclusively to the cerebral cortex and certain of the central ganglia.

The first section, through the genu of the corpus callosum, showed a hæmorrhagic infiltration of the head of the caudate nucleus, which stopped at the margin of the external capsule (fig. 2).

FIG. 2. Vertico-transverse section showing hæmorrhagic infiltration of the cortex and of first anterior part of the caudate nucleus, white matter being intact.

A second section passing a little in front of the anterior limb of the internal capsule showed the same hæmorrhagic lesion affecting frontal cortex, insula, claustrum and the upper two-thirds of the putamen. The body of the caudate nucleus was also much implicated. The anterior division of the optic thalamus, the infundibulotuberal region, the internal and external capsules, the hippocampus and the temporal pole were not involved.

A third section passing by the genu of the internal capsule, the posterior part of the putamen and the anterior part of the red nuclei, showed similar

hæmorrhagic lesions in the insula, ascending parietal, the paracentral lobules and limbic convolutions. The posterior part of the putamen, globus pallidus, posterior limb of internal capsule, locus niger and regio subthalamica were unaffected.

A fourth section passing behind the pes pedunculi, and 3 mm. in front of the splenium of the corpus callosum, showed that the paracentral lobules, superior and ascending parietal, and the præcuneus were much involved. The angular gyrus was slightly implicated. In the neighbourhood of the sylvian fissure the left inferior parietal was affected, but not the right.

FIG. 3. Infarcted appearance of the caudate nucleus (Nissl).

FIG. 4. Fissural hæmorrhage along the outer border of the putamen.

The morbid process was thus almost entirely hæmorrhagic, and limited to grey matter. The maximal lesions were in the anterior segment of the neostriatum, symmetrically on the two sides. The head of the caudate nucleus and the anterior part of the putamen presented an infarcted appearance (fig. 3). It looked like a hæmorrhagic softening without rigorous symmetry; analogous bilateral hæmorrhages involved the frontoparietal cortex. The external capsule escaped, but a linear sheet of hæmorrhage lay along the outer surface of the putamen, reproducing the 'cerebral hæmorrhage of Charcot.' It did not involve the white matter but developed at the expense of the putamen (fig. 4). The claustrum was well outside this lesion.

Histopathology.—A variable aspect was found in the corpus striatum; sometimes only a simple extravasation of red blood corpuscles in the perivascular spaces (fig. 5), sometimes a large extra-adventitial ring (fig. 6). In the latter circumstances, adjoining nervous tissue was necrosed (fig. 7). In sections stained by the method of Loyez a third type of perivascular lesion

FIG. 5. Simple extravasation in the space of Virchow without involvement of extra-adventitial parenchyma (Bielschowsky).

was found, in which hæmorrhage was of minor significance; the vessel was surrounded by a pale aureole, staining less deeply than neighbouring grey matter and with scanty hæmorrhagic effusion (fig. 7). Every grade of lesion was found in proportion to the amount of hæmorrhage and necrosis.

FIG. 6. Paravascular necrosis with hæmorrhagic 'corona' (Nissl).

FIG. 7. Simple paravascular necrosis (Bielschowsky).

These lesions were seen in the caudate nucleus and to a less extent in the frontal cortex, in particular at the level of the first frontal, where involvement was most severe. Perivascular punctiform hæmorrhages were found in all the layers of the cortex, but those most implicated were the fourth, fifth, and sixth (fig. 8). In the cortex the necrotic foci were less numerous

FIG. 8. Paracapillary hæmorrhage in layers 2-6 of the frontal cortex, with cellular necroses (Bielschowsky).

FIG. 9. Paracapillary hæmorrhages of subcortical white matter and of the innermost layer of the cortex; slight changes in cellular architecture (Nissl).

than in the corpus striatum. Cellular architectonic was little modified (fig. 9). In the vicinity of the intracortical hæmorrhages the ganglion-cells were abnormally loaded with lipo-pigment. A certain number showed karyolysis and tigrolysis, not specially typical. Yet at certain spots, particularly at the foot of the sulci, plaques of ischæmic necrosis, well known

in cerebral arteriosclerosis, were characteristically present (fig. 10). No laminal destruction of any important and systematized kind was noted.

In addition, the molecular layer of the cortex showed a large number of pigmentary inclusions, also pigment lying free or enclosed in neuroglial and, in particular, microglial elements (fig. 11). In the neighbourhood of

FIG. 10. Intracortical ischemic necrosis (Nissl).

FIG. 11. Lipopigmentary infiltration of subpial motor cells and of microglial elements of the molecular layer in the vicinity of an intracortical hemorrhagic focus (Nissl).

the hæmorrhagic regions this pigmentary impregnation of the molecular layer continued over a wide extent.

The white matter of the convolutions was as a rule normal. Hunt had to be made over the whole extent of a section to find minute apoplectic foci. At one place, however, in the white matter of the mesial aspect of the superior frontal, we found an area of necrosis accompanied by perivascular demyelination round an axial vessel for a distance of several

millimetres (fig 12). This type of demyelination is exactly comparable to what is currently seen in cases of postvaccinial encephalitis and we direct particular attention to the fact. In our case it was rare, since we discovered it in one place only.

The whole of the cerebral convexity in the vicinity of the superior longitudinal sinus was covered by a hæmorrhagic leptomeninx infiltrated with blood and penetrating into the sulci. A similar hæmorrhagic meningeal state was the sole lesion observed in connexion with the cerebellum. Its grey matter, white matter, dentate and roof nuclei were intact, as were pons and medulla. No appreciable changes were seen in peripheral nerves.

FIG. 12. Perivascular demyelination in the white matter (Loyez).

Thus histopathological examination disclosed no more than a hæmorrhagic diapedesis in relation to small vessels, without inflammatory reaction, involving the grey matter of cortex and neostriatum. The diapedesis was sometimes replaced by a process of occlusion with perivascular necrosis, or by simple demyelination without thrombosis or hæmorrhagic infiltration.

PHYSIOPATHOLOGY.

In view of the negative results of blood culture and of biological examination, it is difficult to interpret the case from a physiopathological standpoint. Whether the toxi-infective cause be rheumatic or not, it had without doubt determined a venous stasis over a wide area of the meningocephalic network, entailing the hæmorrhagic diapedeses already described. Nowhere in the brain were lesions of vascular walls found which could explain

mechanically the appearance of thrombotic or infarctive phenomena in adjoining tissues corresponding to vascular distributions; and in this respect our case supports present-day theories on the origin of cerebral softenings. It seems less and less probable that these are caused by anatomical ischæmia. The researches of Gildea and Cobb, of Wolff and Lennox and others, have shown that inadequate oxygenation, resulting from the stasis, is the cause of distention of vascular walls. The distension is soon followed by parenchymatous œdema with extravasation of erythrocytes and rapid cellular necrosis. This œdema blocks secondarily the blood current coming from neighbouring capillary networks at low pressure. In our case some general cause has induced the distention, which was soon succeeded by the eruption of reds into the arachnoid cisterns, the spaces of Virchow-Robin, extra-adventitial spaces, and even into the cerebral tissues themselves. At certain spots it has been complicated by extensive thromboses of small arteries and veins. Insufficient oxygenation also accounts for the presence of necrotic zones whose topography has already been mentioned.

The elective localization of the morbid processes is no less surprising, for the cortico-neostriatal distribution of the hæmorrhages cannot be explained by anatomical arrangements of the cerebral circulation, so far at least as present knowledge takes us. If the fissural hæmorrhage of the external capsule corresponds to a classical localization, the involvement of the cortico-subcortical grey matter with escape of the white eludes interpretation. The capillary network of the cortex has no terminals and is continuous on the one hand with that of the pia mater (Pfeiffer), and on the other with that of the basal ganglia (Cobb) across the centrum ovale. Then why do we not find the same hæmorrhagic diapedeses in the centrum ovale, where they are seen with the greatest frequency in other affections? It would appear we are here dealing with a toxi-infective agent having a special predilection for the cortico-neostriatal grey matter.

THE CHOREIC SYNDROME.

Has this case any light to throw on the pathology and physiopathology of the choreic syndrome, which are far from being settled despite recent work of much interest? In 1930 Lhermitte and Pagniez published an important paper in which they divided acute chorea into two main types: (1) an inflammatory type, analogous to choreic encephalitis, and (2) a degenerative type characterized by diffuse cerebral lesions associated with marked modifications of the vascular network, distinct from those of inflammatory processes. Their own observation belonged to the second class. The lesions were above all vascular and neuronal. Vasodilatation with pericapillary hæmorrhages was seen, thromboses, vascular ruptures, pronounced changes of cellular architecture with acute ganglionic lesions. The lesions were

diffuse, but Lhermitte and Pagniez mention the particularly severe involvement of dentate nuclei, putamino-caudate segments of the corpus striatum, and of the Purkinje cells of the cerebellum.

A similar distinctiveness is less apparent in the recent case of van Gehuchten combining the inflammatory formula of acute chorea and the degenerative type. In opposition to Lhermitte and Pagniez—who do not reject the idea of two different etiologies for the two types of lesions which they have differentiated—van Gehuchten believes that ‘when an infection is superacute and entails rapid death, the lesions found at autopsy are of a definite infective type (vascular congestion, infiltration, infective nodules, cellular chromatolysis, commencing satellitosis); but when the infection is more diluted . . . a degenerative stage follows the first inflammatory stage; during it inflammatory reactions become progressively less, to disappear in certain cases even when neural degeneration follows.’ Infective forms are always speedily fatal, from a few days to one or two weeks, whereas the degenerative forms evolve over a period of one or two months.

The case which is here described evolved in 36 hours and belongs to the degenerative type, but it does not fit in well with van Gehuchten’s interesting interpretations. Apart from the type of lesions, their topography has to be considered. In the case of Lhermitte and Pagniez, they were mainly dentato-cerebellar and putamino-caudate; in that of van Gehuchten, thalamo-putamino-caudate. This latter topography, with more or less definite involvement of the cerebral cortex, is met with in the majority of reported cases. Our case substantiates in part the conclusions of van Gehuchten, that ‘lesions of putamen, caudate, optic thalamus, complicated perhaps by changes in the cerebral cortex, are alone indispensable for the development of choreic symptoms.’ We say ‘in part,’ for the optic thalamus was normal, while the cortex was involved just as heavily as the neostriatum.

In progressive cases of the type of Sydenham’s chorea it is very difficult to say which are the parts first affected and responsible for the choreic syndrome. Diffuse infections lend themselves very badly to topical differentiation. Only by the critical study of numerous cases with limited localization will it be possible one day to specify the lesions whose incidence determines choreic liberation. No other purpose has been in view in the publication of this case.

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