A CASE OF ACUTE TOXIC CHOREA

BY

R. G. GORDON, BATH, AND R. M. NORMAN, BRISTOL

THE pathogenesis of chorea is by no means established and the exact cerebral mechanism by which the hyperkinesis is determined is still in dispute.

Wilson suggests that the movements are essentially cortical in origin and that they are liberated as a result of interference with one or other afferent path which finally impinges on the cortical motor areas. This theory is tending to displace the older view that chorea is accounted for by a localized lesion in the corpus striatum regarded as an effector discharge centre. Wilson states: 'My summary in respect of choreoathetosis is that it represents a complex type of involuntary movement, for the carrying out of which motor mechanisms of cortical site are requisite. No single and invariable anatomical site for lesions underlying its development is to be expected. It is the expression of disorder of a system. To its continuance afferent cerebello-cerebral defect of regulation contributes and transcortical (volitional) control over its manifestations is very imperfect. As I have on several previous occasions strongly urged, any theory attributing its origin uniquely to striatal destructive lesions is impossible.'¹ So far as the pathology is concerned Minkowski² and Littman³ have adduced pathological and experimental evidence rejecting the striatal theory, while Ziegler⁴ found that Sydenham's chorea was associated with chromatolysis of practically all cells of the central nervous system with swelling of the nuclei and central displacement. Again, Marie and Trétiakoff⁵ in a detailed histological examination of a fatal case of Sydenham's chorea found that changes occurred in all parts of the cerebro-spinal system except (in this case) in the medulla and cerebellum. There is a predilection for the grey matter especially of the cerebral cortex and basal ganglia. The following case is described as a contribution to the subject.

E.A., a young unmarried woman, age 20, by occupation a weaver, was admitted to the Royal United Hospital, Bath, on January 27, 1934. Both she and her sister had been subject to growing pains in adolescence, but otherwise had been healthy with no previous history of chorea.

In December 1932, the patient contracted mumps and had never been well since. She suffered repeatedly from tonsillitis and sore throats. Choreic symptoms started in September 1933, and became very much worse after tonsillectomy in December 1933. Since then she had become more ill, had had no sleep for a week and had been off work for eight days, though for some time previously she had only been able to carry it out with difficulty owing to her involuntary movements.

On admission, she was found to have considerable difficulty in speech and was unable to feed herself owing to a severe degree of choreiform movements especially of the right hand and forearms, lips and eyes. When she attempted voluntary activity the movements became very explosive and violent, so much so that she bruised herself severely. There was no complaint of rheumatic pain, and no demonstrable nodules were discovered.

The apex beat was in the fifth space, $3\frac{1}{2}$ inches from the midline. There was a systolic bruit localized to the apical region, and the pulmonary second sound was accentuated.

At the time of her admission one of us was experimenting on the induction of hyperpyrexia in cases of chorea by hot baths; this was a development from the findings of Sutton⁶ and Bateman⁷ on the effect of hyperpyrexia induced by T.A.B. injections in similar cases. The patient was therefore given a series of baths, the temperature being controlled by a self-recording rectal thermometer. On the first occasion the patient was difficult and inclined to resent the treatment. On the next five occasions, all went well. The patient's temperature rose to 104° F. for 15 minutes, then although the temperature of the bath never rose above 109° F. she maintained a temperature of 102° F. for three hours with very little change in the pulse rate.

On February 4, during the seventh bath, the patient for no apparent reason suddenly stood up, withdrew the rectal thermometer and threw it against the wall. Afterwards she was profusely apologetic for breaking the instrument, and as she was becoming much quieter and sleeping reasonably well, the baths were continued at the same temperature, control depending on intermittent observation of the patient's temperature.

On February 7, she did not seem so well and slept badly. Two days later she was definitely worse and the baths were therefore stopped and nirvanol (3 grs.) was given. Next day she was much worse and was very violent in the evening. Paraldehyde and bromide were given three-hourly and retainers were necessary to keep her in bed. On February 11 she was so violent that nembutal was administered, and this was repeated in $1\frac{1}{2}$ -grm. doses up to 7 grm. altogether before she could be quietened; then she became semicomatose.

Lumbar puncture yielded a clear fluid under slight pressure, of a faint yellow colour, with no clot. Cells, 2 lymphocytes per c.cm.; globulin, negative; protein, less than 0.03 per cent.; sugar, 0.07 per cent.; urea, 0.03 per cent.; Lange curve, 0111110000.

Her temperature then rose to 103° F., and the lung bases became congested. The pupils were contracted equal, and reacted to light. No reflexes were elicited.

On February 13 she died, without having regained full consciousness.

PATHOLOGY

At the post-mortem examination, bronchopneumonia was found at both bases, but otherwise no pathological lesion was discovered outside the central nervous system.

The meninges and brain were very congested and there was marked cortical laceration, especially on the left side, from the separation of the Pacchionian bodies which were larger than normal.

Microscopical Examination.—*Cerebral Cortex.*—Sections taken from the precentral and postcentral areas of the left hemisphere and stained by toluidin blue showed marked swelling of the brain, vascular engorgement and

small subpial hæmorrhages. The nerve-cells exhibited varying degrees of chromatolysis, staining diffusely by this method. The general oedema had disturbed the normal cyto-architectonics of these regions. There was little or no evidence of glial proliferation. No fibre degeneration was observed in sections stained by the Weigert-Pal method. The cortex therefore showed typical changes consequent on general toxæmia, but no specific indication of inflammation or degeneration.

Basal Ganglia.—Thalamus.—Toluidin blue preparations showed swelling and chromatolysis of the majority of the ganglion-cells. It was usual to see about two-thirds of the cell body staining a greenish-yellow colour. When stained by Scharlach R the cells were found to have undergone an advanced

FIG. 1.—Thalamus. Medial nucleus. Chromatolysis, swelling and fatty changes. Toluidin blue $\times 100$.

degree of fatty change, the granules appearing orange-red in colour. Similar findings in the corpus striatum have been reported by Globus⁸ in a case of acute chorea associated with diphtheria of the large intestine. This picture suggests a special susceptibility of the thalamic cells to the toxæmia (fig. 1).

Globus Pallidus.—The majority of the large cells were preserved, staining deeply and showing little differentiation between cytoplasm and nucleus. The fibre system, as shown by the Weigert-Pal method, was unaffected. The neuronc elements, therefore, only showed the results of a severe toxæmia. A very noticeable feature was the presence of numerous giant glial nuclei, the so-called Alzheimer cells. These cells were also found in smaller numbers in the putamen, and scattered among the neurones of the dentate nucleus (figs. 2 and 3). Their appearance in toxic and infective conditions has been noticed by Campbell and Morse,⁹ but is perhaps most constant in pseudo-sclerosis and progressive lenticular degeneration.

Putamen.—The degenerative changes were here much more marked than in the thalamus or globus pallidus. Many of the small ganglion-cells had

FIG. 2.—Globus pallidus. Degenerate ganglion cell and two Alzheimer cells. Toluidin blue $\times 600$.

FIG. 3.—Dentate nucleus. Alzheimer cells. Toluidin blue $\times 600$.

disappeared, while the few large cells visible were in a necrotic condition and contained fatty granules. Satellitosis was frequently present (fig. 4).

Caudate Nucleus.—The changes observed in the putamen occurred here in a more advanced degree. Very few recognizable nerve-cells remained.

Numerous large nuclei containing little chromatin material and no nucleoli were scattered over the field. They were larger than normal astrocyte nuclei, but smaller than the fully formed Alzheimer cells.

FIG. 4.—Putamen. Cell destruction and glial proliferation. Toluidin blue $\times 270$.

FIG. 5.—Red Nucleus. Chromatolysis and glial proliferation. Toluidin blue $\times 80$.

Midbrain.—The cells of the substantia nigra showed only the generalized toxic changes of swelling and diffuse staining. No glial reaction was present. In this situation no defect of myelinization was found in Weigert-Pal preparations. In the *red nucleus*, however, frequent examples of a more advanced

cellular degeneration were visible. Satellitosis was here a prominent feature (figs. 5 and 6). The cerebral crura were normally myelinated.

Dentate Nucleus.—Many cells were in a degenerate condition appearing only as pale shadows in toluidin blue preparations, and Alzheimer cells were present.

SUMMARY OF PATHOLOGICAL FINDINGS

The microscopical examination of various parts of the brain showed a general state of toxæmia affecting all areas examined. The destruction of nerve-cells was most marked in the neostriatum. Fatty substances were

FIG. 6.—Red nucleus. Satellitosis. Toluidin blue $\times 450$.

demonstrated in the ganglion-cells of the thalamus and putamen. The pallidal projection-system was well preserved.

The presence of Alzheimer cells in globus pallidus, putamen and dentate nuclei was observed.

In the midbrain the red nuclei suffered more than the cells of the substantia nigra.

The changes in the cerebral cortex were of a less severe character, and it is clear that a relatively intact pyramidal tract mechanism was preserved for the exteriorization of the hyperkinesia.

There were no signs of tubercular lesions in the Pacchionian bodies, nor were the cell clusters referred to by Winkelman and Eckel¹⁰ as nodules or possible embolic formations seen in any part of the brain examined.

CONCLUSIONS

The above fatal case of acute chorea was presumably rheumatic in origin in view of the absence of any definite inflammatory focus in the body, other

than the terminal bronchopneumonia, and of the very mild degree of perivascular inflammatory reaction, and the absence of exudative and destructive changes in the substantia nigra. The pathological findings agree fairly closely with those described by Freeman,¹¹ viz. : 'The gross picture in rheumatic fever and chorea is altogether like that of any acute infectious disease ; swelling and softness of the brain with vascular injection and occasional small hæmorrhages. Microscopically the alterations in circulation and water balance are corroborated, and there is nothing specific in the alterations of the ganglion-cells. Areas of cortical obliteration are not infrequent. Acute degenerative changes may be especially severe in the locus niger, neostriatum and corpus subthalamicum, but the cortical cells are also said to be severely altered in some cases. There is no reaction on the part of the glia.'

The interesting points in the present case are :—

1. The special susceptibility to the toxin of neostriatum, thalamus, and to a lesser extent the red nucleus and the dentate nucleus.
2. The relative immunity of the cortex and substantia nigra.
3. The almost complete immunity of the cortical and striate projicient fibre system.
4. The presence of definite Alzheimer cells in globus pallidus, putamen, and dentate nucleus.

These are said by most authorities to be characteristic of degenerative changes such as Wilson's disease (progressive lenticular degeneration) and Westphal-Strümpell's pseudo-sclerosis ; but in this case they seem to be associated with a toxic condition, thus confirming the observations of Campbell and Morse.

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