THE EXTRACORTICAL MANIFESTATIONS OF CEREBROMACULAR DEGENERATION

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INTRODUCTION

THE diseases which form this group were formerly believed to be stereotyped as regards their symptomatology. For instance, Collier and Adie¹ stated in 1926 that 'There are few diseases in which the clinical manifestations are so perfectly regular as this malady.' The sentence was written regarding the congenital or infantile variety, but with the description of the juvenile types by Bielschowsky, Spielmeyer, Vogt and others it is now realized that this group of diseases is no rigid and uniform one, but is an extremely varied and curious collection of syndromes.

The degeneration, if such it be, is not limited to the cortex, though cortical signs and symptoms are characteristic of this amorphous group. Nevertheless, superadded cerebellar signs and symptoms have been described by Marinesco² and others. Autopsy reveals extensive degeneration of the cerebellum in such cases. Yet again decerebrate rigidity with concomitant postures, such as flexion of the limbs, labyrinthine and tonic neck reflexes, have been described, notably by Meyer³ and by Van Bogaert, Sweerts and Bauwens.⁴ The causation of such syndromes is presumably the progression of the disease to the caudal end of the red nuclei. Cases do not seem to have been recorded with gross bulbar signs. This is possibly because the involvement of the bulbar structures is incompatible with life. Pathologically, signs of the disease can be found in the cord and even in the peripheral nerves.

With such extensive disease-processes one would hardly expect that cases would not be found which display striatal signs. This is so. In their case Van Bogaert, Sweerts and Bauwens describe a lack of voluntary movements occurring along with the other signs. Again, Marinesco notes that '*Dans la forme tardive, décrite par Bielschowsky, Jansky, Hassin et nous mêmes, il y a des mouvements rythmiques de que même dans ce type on pourrait parler d'une forme hypercinétique*'; and again, in describing a case, he says '*En outre le membre supérieure droit est animé de mouvements à peu près continuel de caractère choreiforme.*' This case showed at autopsy degeneration in the basal nuclei as well as elsewhere. '*Le putamen a un aspect plus clair que le pallidum voisin ; cela provient du fait que les cellules pallidales et la névroglie proliférée contiennent plus les lipoides.*' And in the globus pallidus '*On y voit l'augmentation périnucleaire du protoplasma microglieue, la diminution des prolongements dépourvus d'épines.*'

With regard to the optic signs it is by no means the rule to observe the cherry red macular degeneration in the juvenile types, but a primary optic atrophy is almost invariable. Naville states that '*Le début est insidieux par faiblesses motrices, cécité et démence progressive, atrophie optique, quelquefois rétinite pigmentaire.*' It will be observed in the case recorded below that a generalized pigmented retinitis replaces the usual limited optic signs. That there are transitional types is evident from Goutermann's ⁵ description that '*The changes at the macula consist of a diffuse pigmentation which extends more or less into the surrounding retina.*'

It is difficult to find many references as to the inheritance of the disease. Most writers simply comment on the family incidence. Stenhouse Stewart ⁶ reports a case in which the disease appeared in a number of the members of two generations. The note is very short, but apparently the case is of the infantile variety. Hansen ¹⁶ is of the opinion that a number of factors is needed to produce the typical disease, and ingeniously advances the argument that the abortive, deviating and transitional types are due to a varying admixture of the causative factors. He describes a family in which different types appeared in the different members affected. In Van Bogaert, Sweerts and Bauwen's case the disease appeared in three members of two generations. This certainly does not appear to be suggestive of a Mendelian recessive.

It is interesting to note that in this case (of Van Bogaert) an idiot appeared in the second generation, but lacked the classical signs. Again, in Stenhouse Stewart's ⁶ case there are recorded eight miscarriages in the marriage of an apparently healthy male member of the family. This occurrence was attributed to the fact that his wife was physically defective. The note does not state in what way she suffered. It should be noted that the mother of one of the cases recorded below had two children who died at the age of three months. It would seem to the writer that these accidents are not altogether unrelated. May it not be that those cases most severely affected are represented by miscarriages, those less affected by deaths in childhood, even without any classical signs? The idiot would then represent a stationary case wrecked by the disease.

Regarding the pathology there are three schools of thought. (1) It is an agenesis; for instance, Naville ⁷ says '*Les faisceaux altérés étaient ceux qui se myélinisent le plus tard et il s'agit d'agénésies et non de dégénérescences secondaires.*' (2) The disease is an abiotrophic degeneration of unknown origin—a widely supported but unhelpful view. (3) The disease is related to Niemann-Pick's ⁸⁻¹⁵ disease, with which it is sometimes associated, and is therefore a degeneration secondary to the disease in the reticulo-endothelial system. There is nothing in the present case which supports this theory, in view of the fact that the spleen and liver are not palpable.

It is curious to note how resistive the auditory areas are to the degeneration. How frequently there is a true hyperacusis it is difficult to say. The case recorded below shows some diminution to auditory stimuli.

GENEALOGICAL CHART.

DESCRIPTION OF PERSONAL CASE

HEREDITY.—*Generation 1.*—The writer has succeeded in obtaining an account of the patient's great-grandmother. She is said to have died at the age of 55. She became blind apparently at about the age of 40. She is said never to have been psychotic. Another member of this generation—the patient's great-grand-uncle—is said to have become insane. The writer has tried unsuccessfully to trace this man. He has been assured that there were no signs of blindness in his case. He is said to have died in middle age.

Generation 2.—There were two female members of this generation and no males. One of these females died after being married some time. She never had any children. The other female member of this generation is the patient's grandmother. Neither of these women showed signs of blindness or dementia.

Generation 3.—This generation is a numerous one. No signs of disease can be found except that the patient's father was born with torticollis. The mother of the patient's cousin (who died of cerebromacular degeneration) is a healthy woman. Neither she nor the patient's father shows any retinal degeneration. For the sake of convenience the patient's mother will be described here. She is a rather stout woman, aged 49. She has a divergent strabismus which she states is due to measles contracted as a child.

The patient's father is aged 53. He was formerly a coal carman, but he has been unable to work for years. He suffers from chronic bronchitis and cannot perform heavy work. Apart from his marked torticollis he displays no obvious abnormality.

Generation 4.—There were 17 members of this generation. They are distributed into four families. In two of these families cases of cerebromacular degeneration have occurred. One of these cases is the patient. For purposes of description these families will be called A, B, C and D.

Family A.—The two first-born children in this family died at the age of three months. They were never taken to hospital and no definite diagnosis was reached. 'They just wasted away.' A female member of this generation in this family is alive aged 35. She is married, with one child. The fourth member of this family died in a mental hospital at the age of 18. He is said to have been one month premature. He was breast-fed and walked and talked at the age of one year. His mother says he was 'delicate from birth' and he complained of sickness and headaches from the age of two and a half years. He went to school at the age of five and was apparently healthy. His teacher, however, suggested that he had defective eyesight soon after he started school. He was then noticed to be groping for his knife and fork when at table. He 'groped about when in dark passages' (this is very suggestive of nyctalopia). It was also noted that he tilted his head forwards when looking intently at objects. This may have been due to unequal degeneration in the retina with preservation of the lower fields.

He was taken to an Eye Hospital where he was given glasses. His failure to improve led to his being taken to another hospital where the gloomy prophecy of complete blindness in a year was made. He had diurnal enuresis at the age of six and did not appear to be learning at school. He was transferred to a residential blind school, but soon after he went there he had a fit. He had frequent fits following this. He is said to have known when these fits were due and to have been emotional and stubborn before they arrived. He is said to have cried out and then fallen down. He was never hallucinated, but was seclusive and destructive. Owing to the fits he was returned home from the blind school. He was then sent to an infirmary, certified and sent to a mental hospital. There he is said to have become emaciated and not to have known his relatives. He died at the age of 18.

Unfortunately no proper neurological examination was carried out on this patient, neither was any examination made of his eyes. His death was stated to have been caused by status epilepticus.

Family B.—This family consists of two males, ages 13 and 25 respectively. They are both said to wear glasses for refractive errors, but are otherwise normal.

Family C.—There are five members of this family. One is said to have died from mastoiditis. The others are said to have no signs of illness.

Family D.—Out of the eight members of this family two have exhibited cerebromacular degeneration. One died last year and one is the patient.

The one who died last year was a male. He was a full-time birth, born normally, and breast-fed. He walked early and appeared to be a bright child. He was not sent to school until the age of five. A short time after he went to school he was knocked down by a motor car. Following this accident he started to stutter. He was then found to have defective eyesight at school. He was sent to a municipal home for six months. While he was at this home he had two fits. He slowly deteriorated and the number of the fits increased to average one a day. With the increase of the fits his sight gradually failed and he became totally blind. The fits appeared to be generalized and he was dazed after they occurred. This stuporose condition is said to have lasted as long as three hours. He is said to have 'kept pulling his fingers and his teeth' while in this state.

At the age of 12 years he complained of visual hallucinations at night. One night he complained that he saw a rat and complained that he 'saw things' on other occasions. At last he jumped out of bed and declared that there was a dog after him. He was sent to a local infirmary and thence to a mental hospital. He was admitted there at the age of 14 in December, 1928. He was almost blind and had a slight lateral nystagmus, but no other marked nervous signs. In 1931 he had 71 major epileptic fits. He had a pronounced stutter, while some ataxia and doubtful Rombergism were noted. He was seen by the visiting ophthalmologist, who diagnosed cerebromacular degeneration with retinal degenerative changes.

He died in February, 1932, and no autopsy was allowed.

THE PATIENT.—She was the first-born child of this family. She was a full-time child, normal birth and breast-fed. She seemed rather prone to the usual children's complaints, especially bronchitis. She went to school at the age of three and there she caught measles. She was then kept at home until the age of five when she returned to school. She appeared to be bright and normal until she received a blow on the head at the age of six. It was then discovered that 'she couldn't see to write on the lines at school.' She was taken to a hospital where her eyes were tested and her parents were assured that 'glasses were no good for her.' When she was 12 years old she complained of night terrors but not of hallucinations. She was sent to a residential school, but was returned home at the age of 16, probably because it was found that she could not learn. Even at this time she did not appear to be conspicuously dull and attempted to take part in the domestic work such as scrubbing.

She was kept at home, but at the age of 17 she had her first fit. These fits gradually increased in frequency. According to her mother's statement these fits were preceded by her spinning round and round three times (? epilepsia rotatoria). If not prevented she would fall and hurt herself in

these seizures. When she fell to the ground she 'had convulsive movements and then seemed dazed for a time.' Her tongue was nearly always bitten. Her fits are said to have been identical with those of her brother. When she was 22 she was sent to an epileptic home and was there until three months ago. She was steadily deteriorating. She was suspected of having a post-encephalitic condition while at the Home, the diagnosis being founded on her 'mask-like face, and tremor of lips and tongue.'

FIG. 1.—Note the attitude of the left hand, the facies and the position of the feet.

Owing to her deterioration she was certified and sent to Bexley Mental Hospital three months ago.

Physical Findings.—She is a well-covered woman of 28 years. Her general posture is flexed with bowed shoulders and her hands hanging down before her (see figs. 1 and 2). Her walk is Parkinsonian in type and rather festinate. The nurses state that 'she seems to be tipping forward when she walks.' She does not swing her arms and progresses 'all in one piece' with no rhythm. There are no tremors of her limbs. She makes no unnecessary

movements and displays little emotion. Her facies is interesting. She has a mask-like expression, but the face itself is full and rounded. The colour is rather high and she usually has a flush. (This fresh-coloured, full but mask-like face was also present in the cousin when he displayed the disease. A photograph which was taken at the age of 13 and which the writer was permitted to inspect showed this very clearly. It is quite distinct from

FIG. 2.—This picture gives an impression of animation which is somewhat deceptive. Note the attitude of the left hand and the bowed stance.

features characteristic of the family—the ‘family face’ is rather thin and pale.)

Cranial Nerves.—Olfactory sense is absent. She was unable to distinguish between oil of lavender and assafoetida. She said that they both ‘smelled of nothing.’

She has a very faint perception to a strong electric light if it is shone directly into her eyes. This remnant of her vision is rapidly tired, and

curiously enough she frequently succeeds in perceiving the light if allowed to use both eyes, but if either eye is covered she says at once that she cannot see it.

My colleague Dr. Walker, who is collecting material for a paper on pigmented retinitis, has kindly allowed me to utilize his notes on this case. He states 'The fundi show large bone-corpuscle-like aggregations of pigment in the periphery and extending to an area of one disc-breadth from the disc. The right macular region is clear, but there are a few masses of pigment in the left macular region. Some of the masses of the pigment in both eyes are long, following the line of the blood vessels and have the "bone-corpuscle" masses branching off from them. The choroidal reflex is otherwise pale. The discs are waxy white. The vessels are thread-like and there is no difference between the width of the arteries and the veins.'

The eye movements are normal. She shows no nystagmus on looking towards her hands. The eyes react to light and give a consensual reflex.

The motor trigeminal shows no abnormality, but she has hypæsthesia all over her face. The conjunctival reflex, however, is present on both sides. Taste is completely absent, and she is unable to tell the difference between salt and quinine. She is said to be able to tell the difference between coffee and cocoa, but this is very improbable. There is no perceptible facial weakness. Her hearing appears to be fairly acute. She can hear a watch at the distance of one foot. She hears speech and knows when the gramophone is playing. The ninth nerve appears normal except for the absent sensation of taste over the posterior third of her tongue. The palate moves normally. There is no wasting of the sternomastoids. The tongue protrudes, but not to the full extent. There is a marked tremor. When her tongue is protruded there is a slight tremor in her lips.

Sensory System.—She is a poor witness and it is difficult to be sure if her perception to cotton-wool is diminished or not. With pin-prick she feels the prick, but states that it causes her no pain. Although the pin was stuck into her sufficiently to make her bleed she still denied pain. She has no appreciation of heat and cold and constantly insisted that the hot and cold tubes were the writer's fingers. Her joint sense is diminished both for small and large joints. Her sense of vibration is entirely absent. She managed to touch her index fingers together, and to touch her nose, but the performance was clumsy.

Reflexes.—Her biceps and triceps reflexes are present and equal on both sides, but the supinator jerks were not obtained (although tested on a number of occasions). The knee-jerks are present and equal, but the ankle-jerks are sluggish. There is no clonus. The abdominal reflexes are present and brisk. The plantars are flexor.

Power seems fairly good. There is no wasting nor trophic lesions. There is a poor peripheral circulation and the legs frequently get blue and cold.

She has cog-wheel rigidity which is variable. At times this rigidity is more that of a vague sense of resistance, but at other times it is marked. The festination of her gait varies similarly.

Investigation of Other Cortical Functions.—She is so demented that it is difficult to know how much one can rely on her statements, but the following data are given for what they are worth.

She was unable to identify a matchbox, a thimble, a coin or a pencil by holding them in her hands. She succeeded in identifying a paper, but she may have heard it crackle. She makes no mistakes in words, but she is reluctant to speak and never uses long sentences. It is impossible to test her minutely for aphasia, but this does not appear present with such senses as she has left. She is able to carry out commands such as touching her nose and other parts of her body when requested. She has never learned to knit (an accomplishment usually acquired easily by the blind). This may be due to intellectual difficulties or to slight apraxia. She cannot add two and two together.

Other Systems.—She is rather fat and well covered. There is no abnormal hair distribution. Her lungs are normal. There is a soft systolic murmur at the cardiac apex. It is not markedly conducted. Her blood pressure is low, 70/45. The Wassermann is negative in the blood. The C.S.F. was under low pressure—90 mm. of water (when sitting). After about 10 c.c. were removed it refused to register, but could be raised by Queckenstedt's method. The Wassermann and Lange tests were normal. There was no increase in cells or protein.

The liver and spleen are not palpable.

The patient has had three fits in the last quarter. They showed no unusual characteristic. She displays no interest in her surroundings and sits in the same spot all day. She gives no evidence of hallucinations.

In her case the degeneration appears to involve the polar regions of the cortex, sparing the rolandic and temporal areas. The mask-like facies, the tremor of the tongue and lips, the posture, gait and rigidity are all suggestive of extrapyramidal lesions. The hypæsthesia to pin-prick and temperature may be due to thalamic degeneration. It is interesting to note that in Meyer's case considerable changes were found in the thalami.

All the other members of this family are normal. The writer made a special visit to their home (as well as to the home of family A), and although a detailed examination in the neurological sense could hardly be requested the family kindly allowed him to examine their eyes. No signs of pigmented retinitis were found.

Generation 5.—One member of this generation belongs to family A. Her eyes appear normal, but there is a little fine pigment on the lateral side of the discs. It probably falls within the bounds of normality.

Of the other two members of generation 5 in family D the writer examined the youngest (æ. eight months) and found no abnormalities in the eye-grounds. The elder member, age four, refused to allow her eyes to be examined.

THERAPEUTICS

Apart from preventive measures the writer is unable to find any successful therapeutic attempts mentioned in the literature except those of Vollmer. This experimenter injected an ether-alcoholic extract of brain lipoids and claims that the progression of the disease was arrested. After the cessation of the treatment, he states, the child rapidly deteriorated and died.

A similar experiment, but in this case the peroral administration of raw calf's brain and liver, was made by the same writer. No success was obtained by this method.

These experiments were made on cases of the infantile variety. The writer feels that his case has progressed too far to profit from any therapeutic measure.

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