

## NON-ALCOHOLIC POLYNEURITIS ASSOCIATED WITH KORSAKOW SYNDROME

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THE usual association of polyneuritis with a Korsakow syndrome is that caused by alcohol, and the reason for describing these cases is that a Korsakow type of illness associated with polyneuritis which is non-alcoholic in origin is much less common.

### CLINICAL DESCRIPTION OF CASES

*Case I.*—Patient D.D., æt. 25, married, was admitted on January 15, 1934. The history given was that the patient had had one pregnancy which was uneventful. She became pregnant for the second time, and during this pregnancy suffered from œdema, albuminuria and raised blood pressure. Partly owing to these symptoms and partly owing to the fact that the presentation was a breech, labour was induced on October 4, 1933, at another hospital. The labour was difficult, and almost immediately patient developed a temperature of 103° F. as a result of pelvic infection. This lasted until November 14, when the temperature subsided and she appeared to be progressing favourably until the middle of January, 1934. At this time, she became confused, emotionally unstable, and restless, and was transferred to the Maudsley Hospital.

On admission, she was elated and euphoric, said everything was lovely and addressed everyone as 'darling.' She talked in a rambling manner, was restless, confused, and disorientated. She was also incontinent of urine and fœces. Physically she was thin and 'drawn' and complained of pain in the left leg. The quadriceps on both sides together with all the muscles below the knees was paralysed. The paralysis was of a flaccid type and was more complete on the right than the left side. Patchy anæsthesia to pinprick was present up to the level of the umbilicus, and sensation of touch, temperature, deep pressure and joint sense was abolished in both feet, more so on the right than the left side. She also complained of paræsthesiæ in the form of 'pins and needles' in both feet. The left leg was swollen and œdematous. There was a zone of hyperæsthesia to pinprick present at the level of the umbilicus. Fine horizontal nystagmus to both sides and some slight weakness in the arms were present. The deep reflexes in the legs were completely absent and were markedly sluggish in the arms. A blood count showed 3,745,000 red cells with a colour index of 0.75 and slight anisocytosis and poikilocytosis, the white count being normal. The pelvic organs revealed nothing abnormal.

A few days after admission she developed copious diarrhœa with as many as 20 stools a day. The blood pressure was low (86/50) and tachycardia was present. Repeated bacteriological examination of the stools was negative. The diarrhœa persisted until February, 1934, and until then she was given intravenous salines and glucose. At this time she complained of paræsthesiæ in the hands and the pulse rate had risen to 130. Mentally she remained confused and disorientated and at times was noisy and restless. In addition confabulation was present. A blood count at

this time was normal except for a colour index of 0.85; the cerebrospinal fluid was negative apart from a slight increase of protein to 100 mgm. per cent.

In view of the persistence of the tachycardia and the delirious symptoms a search for a focus of infection was carried out but was completely negative. The right antrum was punctured, as it was regarded as being suspicious on X-ray examination but no pus was found. At no time during her stay in the Maudsley Hospital was there any pyrexia. At the end of March the patient showed a sort of occupational delirium. She mistook identities, said she was being attacked, and was still confabulating. There was also present wasting of the small muscles of the hand with patchy anæsthesia to pinprick. The electrical reactions were normal except that the response to faradism in the small muscles of the right thumb was diminished. In the legs reaction of degeneration was complete in both groups of anterior tibial muscles. At the beginning of April an improvement in her mental state was noted, and this became steadily progressive. At the same time the paresis in the hands began to improve. She was discharged on May 16, 1935, when her mental state was normal, but the double footdrop was still present. She was seen on November 15, 1935, when she was very well mentally, the hands were normal and the left foot had improved considerably. The right foot still showed a marked degree of footdrop, but is responding slowly to massage and electrical treatment.

*Case II.*—Patient M.I., æt. 45, married, was admitted on June 3, 1933. The history given was that three weeks before admission patient had a cold and was admitted to a general hospital for observation as it was thought she might have tuberculosis. This, however, was not confirmed. She had also become depressed, lost weight and complained of pain in the right leg. Whilst in the general hospital she became restless and confused and was transferred to the Maudsley Hospital.

The previous history was negative, and patient had had two pregnancies (12 and 14 years before) without incident. On admission she was restless, mistook identities, said the patients were going to be burnt, and was confused and disorientated. She also showed confabulation. These symptoms were much more marked at night. Physically she was thin and pale, and severe diarrhoea was present. Bacteriological examination of the stools showed *b. ærtrycke* to be present, and the patient's blood also showed agglutination to this organism. She complained of pains and tingling in the legs, and the calves and soles of the feet were tender. Footdrop was present on both sides with wasting of the muscles, the deep reflexes in the legs were sluggish and anæsthesia to pinprick was found in the feet and toes. The right hand and arm were weak, with some wasting of the muscles; the deep reflexes in the arms were diminished, and there was also anæsthesia to pinprick in both hands. The pupils reacted sluggishly to light, while coarse horizontal nystagmus to the left was present. Tachycardia was present (110) and the systolic blood pressure was 115 mm. Hg. The patient showed a low grade type of fever with rises of temperature to 100° F. Bile salts were present in the urine. Patient remained restless, confused, and at times noisy, with considerable memory impairment, until August 30, 1933, when she became quieter and more in touch with her surroundings. Her legs showed little change and the wasting of the intrinsic muscles of the right hand had increased and right wristdrop was present. There was also a tendency to pes cavus on both sides. The kneejerks, however, were now active, but the anklejerks were absent.

Massage and electrical treatment produced steady improvement in the paralysed muscles, and at the same time her mental state became progressively better.

She was discharged on May 5, 1934, with no abnormality except for some residual wasting in the legs.

She attended the Out-patient Department regularly and her legs completely recovered. She remained well, both mentally and physically, until October, 1935, when she became depressed and agitated and it was necessary to send her as a voluntary

patient to her own county mental hospital. She showed no evidence of a Korsakow syndrome or polyneuritis at that time.

*Case III.*—Patient E.J., æt. 37, married, was admitted on May 1, 1928. Two brothers were said to be alcoholic, but the patient herself denied alcoholic excess. In the previous history the only points of importance were that the patient had an attack of diabetes in 1924, from which she recovered in a few months, and that she had suffered from diphtheria twice.

The present illness was said to have started twelve months before admission, and seven weeks ago she complained of numbness of the fingers, and was forgetful and irritable.

On admission she was anxious, irritable, somewhat histrionic in manner, showed considerable memory impairment but no definite evidence of confusion or confabulation.

Physically she was emaciated, walked with a highstepping gait and had a generalized tremor. The leg muscles were weak and wasted and the deep reflexes were absent. Anæsthesia to pinprick and temperature was present in both legs below both knees, and also in the hands. Vibration and joint sense were absent in the legs. The urine, blood sugar and blood count were all normal. The patient discharged herself shortly after admission when her condition was quite unchanged.

*Case IV.*—Patient F.F., single, æt. 17, was admitted on November 13, 1933. The previous history was negative except for an attack of diphtheria at the age of seven, after which she was unable to walk for a few months. The history of the present illness was that four weeks before admission she developed pains down the inner sides of both thighs. Three days later her legs became heavy, felt numb and at times they gave way beneath her, and she was also incontinent of urine.

On admission there was weakness and wasting of both legs with difficulty in walking, which she accomplished on a wide base. The kneejerks were present on reinforcement, and anklejerks were very sluggish. There was patchy anæsthesia to pinprick in the legs, while vibration and joint sense were absent. In addition, bilateral horizontal nystagmus was present. Mentally her memory was somewhat impaired and she was facile and euphoric. She improved rapidly after admission and was discharged on January 27, 1934.

#### DISCUSSION

Case I differs from the other three cases in that it was associated with pregnancy and the puerperium, and will be discussed first.

For some considerable time it was maintained that polyneuritis occurring during pregnancy was due solely to the toxæmia of that state, which was responsible also for other symptoms such as albuminuria, eclampsia, vomiting, etc. Ely<sup>1</sup> described the condition in pregnant women who suffered from excessive vomiting also and ascribed the two conditions to the toxæmia. Other authorities (Ledoux, Dupouy and Courtois) hold this view and have reported recovery from the condition after termination of the pregnancy. Hoffman<sup>2</sup> believes that the polyneuritis is due to toxæmia, and states that the condition occurs most frequently in the first or second pregnancies; it is associated with excessive vomiting and develops after the vomiting ceases in the fourth or fifth month.

More recently various writers have tended to discard the toxæmia theory and subscribe to avitaminosis as being the deciding ætiological factor. At the present time there appears to be some confusion regarding the nomen-

clature of vitamins, particularly vitamin B complex. Vitamin B complex is divided into B, B<sub>1</sub>, B<sub>2</sub>, B<sub>3</sub>, B<sub>4</sub>, B<sub>5</sub>, and B<sub>6</sub>. The existence of the three latter is somewhat doubtful and in any case they are of no importance, as far as is known, in the ætiology of polyneuritis. In this paper, by B<sub>1</sub> is meant the antiberiberi vitamin which is sometimes referred to by American biochemists as B, while by B<sub>2</sub> is meant the antipellagric vitamin which is sometimes referred to as G. Strauss and Macdonald<sup>3</sup> state that deficiency of vitamin B<sub>2</sub> causes the anæmias of pregnancy, and that these in turn reduce gastric secretion and produce vomiting. They maintain that the clinical picture of polyneuritis associated with pregnancy is identical with that of beriberi, and they quote the successful treatment of three cases with yeast (containing vitamins B<sub>1</sub> and B<sub>2</sub>), cod liver oil and iron. Ungley<sup>4</sup> described a familial type of polyneuritis occurring in pregnancy and the puerperium, and found no evidence of vitamin B deficiency. Cowgill,<sup>5</sup> on the other hand, secured relief of symptoms by feeding with vitamin B complex in cases of polyneuritis associated with pregnancy, and he found that in the gastric juice of pregnant women there was deficiency or absence of hydrochloric acid. This produced loss of appetite, which in turn caused avitaminosis with increased loss of appetite, and according to him a vicious circle was set up. Mellanby<sup>6</sup> regards deficiency of vitamin A as an important factor in the development of puerperal septicæmia, but in this case there is no evidence that there was any absence of vitamin A during pregnancy.

It will be seen that there is still considerable doubt as to the ætiology of this condition, and it is probable that several factors may determine the illness.

Thus in Case I there was undoubted evidence of toxæmia during the pregnancy, as shown by the albuminuria, œdema and raised blood pressure. On the other hand, there was no history of excessive vomiting. Secondly, there was the severe infection after the puerperium in the form of a septicæmia, and this may have been an important ætiological factor. After the polyneuritis had developed there was a severe gastrointestinal upset, as manifested by the profuse diarrhœa. This may have resulted, at that time, in an avitaminosis which may have aggravated the polyneuritis which was already present.

It seems impossible to ignore the toxæmia of pregnancy, the septic infection, and possibly the gastrointestinal one also (although no organisms were isolated) as ætiological factors; as already mentioned, too, avitaminosis may have contributed, although there was no direct evidence for this.

Regarding polyneuritis not associated with pregnancy, many authorities also believe that the condition is determined by avitaminosis. Wechsler<sup>7</sup> believes that polyneuritis due to specific factors, such as alcohol, diabetes, etc., may be *determined* by avitaminosis. He states that alcohol attacks the liver and gastrointestinal tract, causing loss of appetite and vomiting, which result in non-absorption or assimilation of vitamins. He also states that diabetics

are deprived of vitamins as a result of their restricted diet, and that the absence of vitamin B<sub>1</sub> or B<sub>2</sub> is the determining factor in all cases of neuritis. Strauss and Cobb<sup>8</sup> agree with this and report more rapid recoveries as a result of prescribing vitamins. Perry<sup>9</sup> advances similar views and states that absence of vitamins A and C may give a clinical picture of multiple neuritis.

Mellanby<sup>10</sup> experimented with puppies, and after feeding them for a period of three to four months on a diet deficient in vitamin A produced degenerative changes in the spinal cord which he demonstrated with Marchi's stain. He stated that the animals showed the same symptoms as those fed on a diet deficient in vitamin B complex, and that the symptoms were aggravated if they were fed at the same time on wheat germ or ergot. If, however, the animals were given vitamin A or carotene, this prevented the effect of the ergot, and he concluded that degeneration of the cord is controlled by two factors, viz. a positive harmful influence or toxin and the absence of a defending mechanism, i.e. vitamin A.

Grinker and Kandel<sup>11</sup> disagree with Mellanby, and maintain that the apparent ataxia is due to weakness and loss of weight, that no corroborative stains for fats other than Marchi's method were used, and that this method often produces artefacts. Grinker and Kandel, however, experimented on rats, in which they were unable to produce changes in the nervous system, although the animals showed loss of weight, weakness and ataxia, which cleared up on feeding with vitamin B complex. They also fed monkeys on a diet deficient in vitamin A and were unable to show any definite degeneration of the central nervous system. They concluded that vitamin deficiency does not produce degeneration of nerve-fibres, although its effect on ganglion-cells of the central nervous system ('central neuritis' of Adolf Meyer) may, if the duration is long enough, endanger the existence of many nerve-fibres and the vascular damage may eventually produce secondary ischaemic effects. Zimmerman<sup>12</sup> found it difficult to produce neurological deficiency of vitamin B complex in rats and thought they stored this to such an extent that it was impossible to deplete them, whereas in dogs marked peripheral polyneuritis of a purely degenerative type affecting the myelin sheaths could be produced. Von Hofmeister,<sup>13</sup> on the other hand, showed that polyneuritis can result in rats from deficiency and not absence of the antineuritic vitamin.

It will be seen that the question as to how far avitaminosis can determine degeneration in the nervous system is still a very open question. In Case II of the series there was, firstly, the history of infection with a cold, and, secondly, the gastrointestinal infection with *b. ærtrycke*. As in Case I, it is possible that the polyneuritis may have resulted from the *ærtrycke* infection and may have been aggravated by avitaminosis resulting from the profuse diarrhoea.

In Cases III and IV there were no obvious aetiological factors, except that in Case III there was a history of an earlier attack of diabetes, although there

was no clinical or laboratory evidence of this while the patient was in hospital. In Case IV the only factor present was that the patient had had an attack of diphtheritic polyneuritis at the age of seven, and it is a well-recognized fact that one attack of polyneuritis leaves a predisposition to a further one.

At the present time it would appear undesirable to dogmatize as to the ætiology of these cases, and best to retain an open mind and to regard both the toxic and deficiency factors as being important.

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