changes in extrapyramidal symptoms without the addition of potassium or carbohydrate supplements.²³ Drowsiness, euphoria, and nystagmus have been attributed to the addition of potassium or carbohydrate supplements.²³ The major pathway of tryptophan metabolism via tryptophan pyrrolase is known to be induced by tryptophan loading and by the effects of large pyridoxine supplements.²⁶ Increased adrenocortical activity is common in depression, and Rubin²⁷ has presented evidence that increased handling of tryptophan through the tryptophan pyrrolase-kynurenine pathway occurs in depression. Both substrate induction and hydrocortisone induction of tryptophan pyrrolase are to be expected, therefore, when large doses of tryptophan are given to depressed patients. A study of the antidepressant effect of tryptophan together with an inhibitor of tryptophan pyrrolase such as allopurinol²⁸ would be of interest.

L-tryptophan compound tablets were obtained from Cambrian Chemicals Ltd., Croydon, United Kingdom.

REFERENCES

3. Fare, C. M. B. ibid. 1963, ii, 527.

References continued at foot of next column

ENCEPHALOMYELITIS RESEMBLING BENIGN MYALGIC ENCEPHALOMYELITIS

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Summary

Four cases of encephalomyelitis resembling benign myalgic encephalomyelitis are reported. A Coxsackie B2 virus was isolated from the cerebrospinal fluid in one case and an echovirus type 3 virus from the faces and the cerebrospinal fluid in another. Serological tests indicated Coxsackie B2 and Coxsackie B5 infection in the other two cases.

Introduction

In the past 4 years more cases of encephalitis than usual have been seen in the unit. In general the clinical picture has been variable and non-specific. No virus has been incriminated, except in four cases which further stand out because of their clinical resemblance to one another and to benign myalgic encephalomyelitis. Laboratory evidence indicates enteroviral infection in these four cases. Only three cases of aseptic meningitis were seen during the same period; in none was a virus isolated, nor did serological tests indicate a likely virus.

Benign myalgic encephalomyelitis is well documented and the literature has been reviewed by Acheson.¹ A viral aetiology has not been proved. Lately, its entitlement to recognition as an "organic" disease has been questioned.² The cases here described presented at intervals of some months; they did not arise in a closed community; all were males; there was no poliomyelitis "scare" at the time.

Case-reports

FIRST CASE

Whilst in Arctic waters a 34-year-old ship's officer was taken suddenly ill with dizziness, low-grade pyrexia which lasted for two days, and vomiting and diarrhoea which persisted for 10 days, although loose stools were to trouble him for many months. On the second day he had an occipital headache and a left-sided facial palsy. He continued to feel irritable and profoundly depressed; memory for recent events was poor; powers of concentration were impaired. He described three types of headache occurring in bouts—a constant dull ache, violent stabs of pain, and circumscribed patches of scalp pain. Alcohol, even in small quantity, promptly induced headache. He slept poorly at night but tended to sleep by day. 4 months later he developed pain and "flickerings" in the quadriceps, right facial, neck, and shoulder girdle muscles; the flickerings were worse after exercise. He became unsteady on his feet.

References—continued

feet, tended to trip over objects, and was glad to rest after walking fifty yards. 2 weeks later he had slight paraesthesia in the left upper limb and a band of paresthesia round the chest.

On clinical examination in the fourth month of his illness he was found to have a left-sided facial palsy of lower-motor-neurone type, fasciculation of the right facial, neck, and shoulder-girdle muscles, and a coarse tremor of both hands. Full blood-count was normal. The erythrocyte-sedimentation rate was 2 mm. in the first hour (Westergren). The electroencephalogram was normal. The cerebrospinal fluid was under normal pressure; the protein content at 64 mg. per 100 ml. was just above the upper limits of normal (60 mg. per 100 ml.) for our laboratory; the gamma-globulin fraction at 4.2 mg. per 100 ml. was not increased; there was no increase in cells. No virus was isolated from the faeces but a Coxsackie B2 virus was grown from the cerebrospinal fluid in H.Ep.II tissue-culture cells.

Relapses characterised by headache, depression, reversal of sleep rhythm, muscle fasciculation, and motor weakness, have gradually become less frequent and less severe. Now, 3 years later, he still tires easily. Though still subject to headaches, they are no longer incapacitating. He still has a coarse tremor of both hands. He has lost 21 lb. (9.5 kg.) in weight although appetite was never noticeably impaired.

SECOND CASE

A 44-year-old doctor, who had had contact with case 1 4 months before, suddenly developed an influenza-like illness with mild pyrexia, nausea, anorexia, and weakness "from the waist down". He had odd feelings of detachment and unreality. Sleep was disturbed by bizarre dreams. Apart from continuing lethargy he seemed to recover in a few days. On rare occasions he noted fasciculation in various muscles. In the fourth month he suddenly developed cramping pains in the calf muscles. Pain subsided in 3 weeks but his left leg continued to feel heavy and tended to drag. He developed attacks of "restless legs", followed, in an hour or two, by intense fasciculation of the leg muscles. Bouts of fasciculation might last for some hours and were invariably followed by severe weakness of the legs lasting several days. On rare occasions he experienced cramping pains and fasciculation in the muscles of the upper limbs and even in the temporalis muscles. On several occasions he experienced sensations in the muscles which he thought might be fibrillation. In this he was probably correct since wasting of the quadriceps muscles shortly became apparent. A striking feature was the abruptness with which severe weakness of the lower limbs might develop whilst walking. Such weakness was invariably followed by intense fasciculation. Reasonable motor function was restored by half an hour's rest. In the fifth month of the illness he developed headaches of three types, a constant low-grade background ache constant dull background headache, periodic patches of scalp pain, and occasional severe stabbing pains. His neck felt stiff. He had had to forego alcohol because of the headache it promptly induced. He complained of muscle pains, first experienced in the acute phase of his illness, and of "flickerings" in his muscles, especially after exercise. His limbs felt weak, yet on putting them to test he had found that they were apparently strong enough, although he was incapable of sustained effort. On occasion he had experienced vague paresthesia in both hands.

On clinical examination in the fourth month of his illness muscle fasciculation and an apparent inability to carry muscular effort were the only abnormalities detected. Full blood-count was normal. The erythrocyte-sedimentation rate was 1 mm. in the first hour (Westergren). The electroencephalogram was normal. The cerebrospinal fluid was under normal pressure; there was no increase in cells; protein content was just within normal limits at 59 mg. per 100 ml. No virus was isolated from mouth washings but an echovirus type 3 was grown from faces and cerebrospinal fluid in monkey-kidney tissue-culture cells.

Follow-up over a period of 2 years has produced the now familiar story of relapse and remission with the trend toward improvement. The only new complaints have been of a bad taste in the mouth during some relapses and of a morbilliform rash on the face and scalp in the eighth month of the illness. Although appetite has been good he has lost a considerable amount of weight.

FOURTH CASE

Within the space of a fortnight all three children of a 42-year-old doctor developed a brief pyrexial illness with headache, sore throat, and vague abdominal pain. Their father had a similar illness with, in addition, a persisting pink-stained mucopurulent postnasal discharge. He felt irritable and profoundly depressed. Within 3 days he developed fasciculation of the calf muscles; this spread to the trunk, upper limbs, face, and tongue. Fasciculation was intense and was always more severe after exercise. ("When fishing I could feel my calf muscles quivering against the interior of my gum boots.") His muscles ached; his handwriting became less legible; he had difficulty in carrying heavy objects and in climbing stairs. Sleep was disturbed, and early-morning insomnia was troublesome. Vague generalised headache had been present from the outset; in the fourth month he developed sharp stabbing headache in the morning, and diarrhea with black stools. Sleep was provoked.

On clinical examination in the fourth month of his illness widespread muscle fasciculation was the only abnormality detected. Full blood-count was normal. The erythrocyte-sedimentation rate was 8 mm. in the first hour (Westergren). No virus was isolated from mouth washings or stool. Paired sera submitted at an interval of 2 weeks gave

Relapses have followed remissions for over 2 years now although relapses have become less frequent and less severe. There is still some residual weakness of the lower limbs. Exercise still provokes fasciculation. He still fatigues readily. During his illness he lost 21 lb. (9.5 kg.) in weight although appetite was apparently unimpaired.

THIRD CASE

Whilst in Germany a 32-year-old jeweller had "influenza" with high fever, profuse sweating, headaches, dizziness, vomiting, and diarrhea with "black stools". Sleep was disturbed by "wild dreams". He had difficulty in focusing and could not walk in a straight line. His limbs trembled uncontrollably. The acute phase of the illness lasted 10 days but he continued to feel profoundly depressed. He fatigued readily and found it difficult to concentrate. Nightmares persisted; he slept badly at night yet was ready to sleep by day. He described three types of headache—a constant dull background headache, periodic patches of scalp pain, and occasional severe stabbing pains. His neck felt stiff. He had had to forego alcohol because of the headache it promptly induced. He complained of muscle pains, first experienced in the acute phase of his illness, and of "flickerings" in his muscles, especially after exercise. His limbs felt weak, yet on putting them to test he had found that they were apparently strong enough, although he was incapable of sustained effort. On occasion he had experienced vague paresthesia in both hands.

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neutralising titres of 1024 and 512 for Coxsackie B5 virus, reported as consistent with recovering infection. Serological tests did not indicate recent infection by any other common virus. He did not have further investigation.

The only new development has been a patch of vague paraesthesia, persisting for a few days, on the dorsolateral aspect of one foot.

Discussion

In many respects these four cases resemble benign myalgic encephalomyelitis, yet it seems that all four initially had an enteroviral infection. Varying combinations of the symptoms and signs here described have been recorded previously in the neurological syndromes attributed to enteroviral infection. An increase in cells and protein in the cerebrospinal fluid is the rule. However, lumbar puncture in the cases in this series was not carried out until referral in the fourth month of the illness. In the past, enteroviral illnesses have been regarded as illnesses of short duration. The isolation of an enterovirus from the cerebrospinal fluid in the fourth month is in itself remarkable; any suggestion that such an illness may last 2 or 3 years demands drastic revision of present concepts.

The clinical picture in enteroviral infection may give little indication of the virus responsible, but the similarities in these four cases are remarkable. Either we accept that different viruses can produce the same clinical picture or we must seek some other explanation. It could be that all were infected by a common virus, the entero-viral infection being fortuitous. (Other cases of encephalitis were seen during this period; none resembled these four; in none was laboratory evidence of viral infection obtained.) It seems less likely that a dual viral infection is necessary for the production of this syndrome.

Could it be that enteroviral infection, in predisposed or previously sensitised subjects, sets in train some process, say of an allergic nature, which accounts for the similarity of symptoms and the chronic relapsing course? This would be analogous with the Guillain-Barré syndrome, reputed to follow infection by a variety of viruses, including the enteroviruses. It may be relevant that 8 years before his illness, patient 2 felt bemused. On the next day he developed vague paraesthesia of the face and left leg. He dismissed these symptoms as unworthy of the profession but severe form after the second dose, the more especially because it is difficult to obtain a sufficient number of metaphases. The few benign tumours which have been examined have generally shown a normal diploid mode.2-4

We saw a case of recurrent meningioma in May, 1968. The tumour was thought to have been completely removed, and there was no histological evidence of malignancy. Cytopathetic studies, however, showed striking hypodiploidy and three structurally abnormal chromosomes in every metaphase. Thus, from cytopathetic findings the tumour was thought to have undergone malignant transformation. When it recurred 18 months later, the meningioma now also revealed definite histological malignant changes.

Case-report

A meningioma was removed from a 70-year-old man in 1965. He did well until May, 1968, when he became weak and tired. He noticed increasing paraesthesia of the hands and feet, and headaches of increasing frequency. The headaches had been increasing in severity for a year. The paraesthesia had continued, and became severer in the left hand. He had a stiff neck and his left arm was paralysed. He had difficulty in swallowing and speech was slurred. He was incontinent of urine and faeces, and there was a patch of vague paraesthesia of the face and left leg.

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