PRELIMINARY COMMUNICATIONS

Possible Association between Triphasic E.E.G. Waves and Disorder of Dopaminergic Systems

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Summary

In a patient probably suffering from Jakob-Creutzfeldt disease of the Jones-Nevin type and in another with a cerebral infarction treatment with amantadine (Symmetrel) 100 mg twice a day caused repetitive triphasic waves to disappear from the E.E.G. in each case. In view of these findings and the fact that some other conditions in which repetitive triphasic E.E.G. waves are a clinical feature greatly improve on treatment with levodopa, the suggestion is made that these waves result from a disorder of the dopaminergic system.

Introduction

Abnormal triphasic complexes in the form of repetitive sharp waves are seen in the electroencephalogram (E.E.G.) in various diseases, but the cause of the abnormality is not properly understood. From observations of the results of amantadine treatment in patients with triphasic E.E.G. waves we believe that they are due to a disorder of the dopaminergic system.

Triphasic Waves and Amantadine

Braham (1971), reporting the results of amantadine therapy in a case of Jakob-Creutzfeldt disease of the Jones-Nevin type, found that it dramatically improved the patient's condition and that the sharp-wave pattern in the E.E.G. disappeared. Our experience with similar cases has been the same as Braham's.

One of our patients who had a rapidly progressing dementia and was comatose, and was probably suffering from Jakob-Creutzfeldt disease, fully recovered consciousness when given amantadine (Symmetrel) 100 mg twice a day and was able to sit up and eat unaided, though the dementia remained. The triphasic waves initially present in the E.E.G. completely disappeared two days after amantadine therapy was started (fig. 1). When it was stopped and ephedrine 50 mg three times daily was substituted the patient relapsed into coma and the triphasic waves reappeared in the E.E.G. The ephedrine was given in order to discover whether the improvement on amantadine was merely due to an arousal action, but clearly it was not.

Another of the patients to whom we gave amantadine was suffering from an acute hemiplegia as a result of a cerebrovascular occlusion. The E.E.G. (fig. 2) showed repetitive triphasic waves on the side of the infarction, though they were not so continuous as those usually seen in cases of Jakob-Creutzfeldt disease of the Jones-Nevin type. The triphasic waves completely disappeared when amantadine was given but reappeared when it was stopped.

FIG. 1—E.E.G. record of a woman probably suffering from Jakob-Creutzfeldt disease (Jones-Nevin type). First part shows triphasic waves; patient was comatose. Second part, recorded two days after start of amantadine therapy, shows much improvement; patient able to eat unaided. Third part, recorded after amantadine had been stopped and ephedrine substituted, shows a return of triphasic waves; patient was again comatose.

FIG. 2—E.E.G. record of a patient suffering from right-sided haemorrhagic infarction. First part shows triphasic discharge in right frontal area. Second part, recorded after start of amantadine therapy, shows much improvement, with disappearance of triphasic waves. Third part, recorded after amantadine therapy had been stopped, shows a return of triphasic waves. Hemiparesis remained unaltered. (Note: paper speed was twice that of E.E.G. in fig. 1.)

Discussion

We have found that repetitive triphasic E.E.G. waves may be seen in the following conditions: Jakob-Creutzfeldt disease (Jones-Nevin type); hepatic coma (in cases of portocaval shunt)*; late infantile form of amaurotic idiocy (Pampiglione and Lehovsky, 1968); Parkinson's disease associated with accidental hypotension (Gubbay and Barwick, 1966); cerebral infarction; cerebral haemorrhage; and large subdural haematoma in old people. There are probably others.

The first four of the above conditions have in common the clinical features of coma and hyperkinesia, mostly in the form of myoclonus. Furthermore, Jakob-Creutzfeldt disease (Jones-Nevin type) improves on treatment with amantadine, hepatic coma improves on treatment with levodopa (Parkes *et al.*, 1970), and Parkinson's disease is often beneficially treated with a combination of levodopa and amantadine. The essential disorder in Parkinson's disease is a failure of the dopaminergic system, and the object of treating it with a combination of levodopa and amantadine is to raise the level of dopamines. Therefore, the value of amantadine and levodopa in the treatment of Jakob-

* In cases of hepatic coma repetitive triphasic E.E.G. waves are absent or occur less often in patients who have been taking neurotrophic drugs such as phenobarbitone, diazepam, or promethazine before the onset of coma (Schwartz and Seguy, 1970).

Creutzfeldt disease and of hepatic coma is probably also due to a compensating action in the presence of a disordered dopaminergic system. Taken together, these findings suggest that triphasic waves occurring repetitively and regularly in an E.E.G. are caused by a disturbance of the dopaminergic system.

The question arises whether the hyperkinesia and the coma are caused by disorders of two separate dopaminergic systems. The following considerations support such a view. (1) In the early stages of Jakob-Creutzfeldt disease of the Jones-Nevin type the triphasic wave E.E.G. picture may occur in association with myoclonus but without a disturbance of consciousness. (2) In some cases of slowly developing cerebral infarction myoclonus is an early feature but there is no loss of consciousness. Myoclonus disappears when the patient becomes hemiparetic, which is understandable when it is remembered that Parkinsonian tremor may disappear when a lesion of the internal

capsule occurs. (3) Triphasic waves may appear in a case of rapidly developing hemiplegia without loss of consciousness and disappear after the administration of amantadine.

More supporting evidence is needed before this concept of the cause of triphasic E.E.G. waves can be accepted, and it is to be hoped that this communication will stimulate further investigations.

References

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MEDICAL MEMORANDA

Bilateral Renal Carcinoma associated with Polycystic Kidneys

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The frequency with which renal carcinoma develops in polycystic kidneys is not accurately known, but on reviewing the literature it appears to be more common than usually credited. The purpose of reporting this case is to remind clinicians of this complication, which is particularly important because of the longer survival of patients with this condition due to improvements in the treatment of hypertension and chronic renal failure. It raises the question of how early bilateral nephrectomy should be considered in these patients.

Case Report

The patient, a 44-year-old accountant, was admitted to the Radcliffe Infirmary with a three-month history of malaise and night sweats. For five days he had been vomiting and suffering from colicky, hypogastric pain. He was known to have had bilateral polycystic kidneys for 16 years and had been treated for hypertension with methyl dopa during the previous three years. There was no family history of polycystic disease. Over the previous year he had had, for the first time, several bouts of haematuria.

On examination he was found to be pale, dehydrated, and unwell, with a fever of 38.3°C and bilateral ankle oedema. The pulse was 92/min, sinus rhythm, and the blood pressure 120/80 mm Hg, with a pulmonary systolic ejection murmur. No adventitious sounds were heard in the lungs. Abdominal palpation showed massive enlargement of both kidneys, more marked on the right side, where the lower pole was fixed. Blood urea was 82 mg/100 ml, and I.V.P. showed loss of the middle calices on the right side with calcification in the renal shadows. Renal angiograms showed increased, abnormal vascularity in the middle of the right kidney, indicative of a neoplasm. Chest x-ray examination showed bilateral nodular tumour deposits in the lung fields. In view of these findings he was treated with medroxypro-

gesterone 100 mg twice daily. His condition deteriorated, however and he died three weeks later.

NECROPSY FINDINGS

The body was that of a thin, pigmented man with abdominal distension. Internal examination showed no abnormality in the brain. The lungs contained scattered, discrete, rounded tumour nodules in all five lobes. The heart showed mild left ventricular hypertrophy. The kidneys were grossly enlarged due to polycystic disease. The left kidney (fig. 1) contained a partly encapsulated haemorrhagic tumour 6 cm diameter in the upper pole (a). Opposite the middle calices was a 2-cm, grey, solid nodule of tumour tissue (b). The middle portion of the right kidney (fig. 2) was virtually replaced by an irregular, grey,

FIG. 1—Left kidney showing two foci (a and b) of tumour infiltration. FIG. 2—Right kidney showing two foci (c and d) of tumour infiltration.