Joint Meeting No. 3

Clinical Section

President F B Gibberd FRCP

with Section of Psychiatry

President Richard Hunter MD

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Cases

Motor Neurone Disease and Dementia: Probably Creutzfeldt-Jakob Disease

R M Sherratt MRCP
(for F B Gibberd FRCP)
(*Queen Mary's Hospital, Roehampton, London SW15 5PN*)

J V L, man aged 53

History: Discharged from the army after World War II with a disability pension for shrapnel wounds and a psychiatric breakdown. He was seen at Belmont Hospital in 1951 and 1953 where a diagnosis of a chronic anxiety state in a psychopathic personality was made. In 1958 he was seen at University College Hospital for further evaluation of anxiety and an abnormal EEG was recorded. The possibility of myoclonic epilepsy was considered. In March 1972 motor neurone disease was diagnosed on clinical and electromyographic grounds.

In August 1973 he began wandering the streets inappropriately dressed, set fire to his room with cigarettes several times and was admitted to hospital for observation and care. Between September and December 1973 the signs of motor neurone disease, especially the fasciculation, progressed from involving the shoulder muscles to those of the arms, anterior and posterior chest wall and the thigh muscles. In addition, in the biceps and finger flexor muscles, myoclonic jerks were noted occurring about once in every five seconds. There were no sensory signs. Coordination was good and there was no ataxia on formal testing. No visual defects or defects in ability to concentrate urine were found. In September 1973 the mental state was characterized by a blunting of sensibility in ward social situations, impairment of mental arithmetic and abstract reasoning, the Wechsler adult intelligence scale IQ being 66 (verbal) and 63 (performance). By December 1973 there was echolalia, inability to reason or to perform any mental arithmetic, though spatial and temporal orientation was preserved. The psychometric tests were impossible to carry out owing to his poor mental condition.

Investigations: EEG (27.9.73): posteriorly, poorly formed and sporadic alpha rhythm at 7.5–8 Hz disturbed by theta potentials at 4–6 Hz occurring either diffusely or in long synchronous runs. Intermittent monophasic medium voltage sharp waves occurred synchronously, maximal in the postcentral region, possibly more marked on the right. Although there was no clear periodicity these tended to occur in clusters at one- or two-second intervals and when the patient was alert. Photic stimulation produced better responses at single flash frequencies of one or two per second.

EEG (9.11.73), with EMG electrodes applied to the left biceps and right biceps muscles: this record was similar to the first but the sharp waves were more persistent and often of higher voltage. Some myoclonic jerks were synchronous with the sharp waves, but others were independent of them. The small intermittent synchronous sharp waves are characteristic of Creutzfeldt-Jakob disease.

Comment

The description of the 1973 EEGs tallies almost exactly with the description of an EEG done in 1958 at University College Hospital where mention was made of synchronous sharp wave discharges. These were associated with myoclonic jerks, sometimes synchronous and sometimes not synchronous with them.

A resurgence of interest in the Creutzfeldt-Jakob syndrome has taken place following the demonstration by the American workers (Roos *et al.* 1973), that there may be two distinct forms of the disease. One is transmissible to chimpanzees by the technique of inoculating human brain biopsy material into experimental animals,

thereby producing in the affected chimpanzees a clinical picture and pathological findings similar in nature to those in the human subject. In the other form, the inoculation of material from cases of Creutzfeldt-Jakob disease has not produced the syndrome in chimpanzees.

The age and onset of the signs and symptoms in this patient are consistent with a diagnosis of Type 1b Creutzfeldt-Jakob disease. The EEG abnormality and the myoclonic jerks present fifteen years previously are extremely unusual in that so protracted a course for this complaint has probably not been recorded before.

REFERENCE
Roos R, Gajdusek D C & Gibbs C J (1973) *Brain* 96, 1–20

Dr P Rudge said that it would be interesting to inoculate a chimpanzee with cortical tissue from this man. Many workers, particularly in the United States, believed, in his opinion incorrectly, that all the variants of Creutzfeldt-Jakob disease had a similar etiology. It was clear, however, from the paper by Roos *et al.* (Roos R, Gajdusek D C & Gibbs C J 1973 *Brain* **96**, 1–20) that only the Nevin-Jones variant had been transmitted (Nevin S, McMenemey W H, Behrman S & Jones D P 1960 *Brain* **83**, 519–563). This variant was characterized by a rapid deterioration, pronounced myoclonus, a typical EEG appearance at some time in the course of the disease, absence of lower motor neurone involvement and marked spongiform change at post-mortem. Two cases by Roos *et al.* (1973) were said to have had lower motor neurone involvement but the evidence was unconvincing. In one case fasciculation in the left gastrocnemius was cited as evidence and in the other there was said to be pronounced fasciculation clinically but the anterior horn cells were normal at post-mortem. If the present patient's disease could be transmitted this would be very good evidence of Creutzfeldt-Jakob disease being a single entity, as he showed unequivocal evidence of anterior horn cell disease. Why not send some material to Gajdusek?

Alcoholic Dementia

W J W Mallinson MRCP[1] (for B I Hoffbrand MRCP)
(*Whittington Hospital, London N19*)

Mrs V W, aged 53

History: Admitted to hospital in August 1973. A story of increasing confusion and unsteadiness over the preceding six weeks was obtained from a friend; the events immediately preceding her admission have never been clarified. Subsequently a story was obtained of longstanding heavy alcohol consumption (mainly beer).

On examination: Wasted; extensive bruising of the limbs; clinically dehydrated; temperature 36°C. Pulse and blood pressure were unrecordable. Scattered rhonchi were heard in the chest. Liver enlarged by 5 cm; no signs of hepatocellular failure. Comatose – responding slightly to painful stimuli. Fundi were normal. No signs of meningism. The limbs were flaccid and areflexic with flexor plantar responses.

Investigations: Hb 9.2 g/100 ml; MCV 110 μm^3; film showed macrocytosis; platelet count normal. ESR 48 mm in one hour (Westergren). Prothrombin ratio 1.1:1. Serum B_{12} 340 pg/ml. Serum folate 3.2 ng/ml. Plasma urea 105 mg/100 ml, electrolytes normal. Blood sugar normal. Wassermann reaction negative. CSF (traumatic tap): WBC 5/mm^3, RBC 405/mm^3, protein 48, sugar 92 mg/100 ml. Skull X-rays normal. EEG showed a mild generalized abnormality suggesting diffuse cerebral disturbance.

Progress: The patient improved initially with intravenous fluids; nystagmus and paresis of lateral eye movements then became apparent. A diagnosis of Wernicke's encephalopathy was made on the basis of these signs, and treatment with parenteral thiamine commenced. She rapidly regained consciousness and eye signs also improved. Subsequently she was grossly ataxic with persistently absent reflexes; the ataxia has improved so that she can now walk and feed herself. She remains disorientated, and there is marked loss of recent memory. The anæmia has responded to treatment with folic acid.

Comment

This patient exhibits the classical features of the Wernicke-Korsakoff syndrome and has responded to thiamine treatment in the expected manner. She is left with severe intellectual damage; improvement in this respect, if it occurs, is likely to commence in the period from three months to two years after the onset of the illness (Victor *et al.* 1971).

Thiamine deficiency has been established as the most important factor in the genesis of the Wernicke-Korsakoff syndrome, both by clinical observations of the response to treatment (Phillips *et al.* 1952), and by animal experimentation. Cases have, however, been described with normal blood thiamine and transketolase levels only responding to multivitamin preparations and good diet (Cole *et al.* 1969).

The clinical and pathological changes associated with other syndromes of alcoholic neurological disease (peripheral neuropathy, amblyopia, cerebellar degeneration, central pontine myelinolysis and Marchiafava-Bignami disease) have been described in non-alcoholics with a background of malnutrition. It therefore seems likely that they

[1]Present address: St Bartholomew's Hospital, London EC1