'Epidemic neuromyasthenia' 1955-1978

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Summary

A record of fifty-three patients admitted to the Infectious Diseases Department of the Royal Free Hospital between April 1955 and September 1957 suffering from 'epidemic neuromyasthenia' establishes the fact that the condition was endemic in the general population before, during and after the outbreak among the staff of the hospital. A further outbreak occurred in North Finchley between 1964 and 1967 and sporadic new cases are still being encountered. The majority of these patients show evidence of involvement of the central and sympathetic nervous systems and the reticulo-endothelial system. Abnormal muscular fatigability is the dominant clinical feature and it is suggested that mitochondrial damage may provide an explanation for this phenomenon. Enzyme tests carried out in seven cases show pathologically high levels of lactic dehydrogenase, and glutamic oxalo-acetic transaminase. A follow-up study suggests that there is one group of patients that recovers completely or nearly completely, a second that recovers but is subject to relapses and a third that shows little or no recovery, these patients remaining incapacitated.

Introduction

'Epidemic neuromyasthenia' occurred in Dalston, Cumberland, in February 1955 but the author and his colleagues were not aware of that when they began to admit a series of very puzzling cases in April of that year.

An account of the first eight of these was published (Ramsay and O'Sullivan, 1956). After an onset which took various forms but chiefly upper respiratory catarrh, gastro-intestinal disturbances (with nausea and vomiting), or acute vertigo, there followed severe headache accentuated by movement, nuchal pain, pain in the limbs, back, or chest, giddiness, extreme lassitude and paraesthesiae. Muscular cramps and twitchings, pain referred to the ears and transient or persistent tinnitus were features of many cases. Cervical gland enlargement was found in seven cases, various degrees of neck stiffness, pareses and exaggerated tendon reflexes in six;

objective sensory impairment and muscle tenderness in five; cranial nerve palsies in five, extensor plantar responses in three, nystagmus in two and diplopia in two. Later, the details of the first thirty-four cases admitted to the Unit (with very similar findings) were reported (Ramsay, 1957).

Records have been traced of fifty-three patients of whom sixteen were seen in 1955, eighteen in 1956 and nineteen in 1957. Only thirteen of these were from the hospital staff, namely nurses, ward maids or students from the geographically adjacent preliminary training school. Despite difficulty in deciphering the names and addresses of all the doctors who referred these cases with diagnosis of poliomyelitis, meningitis and pyrexia of unknown origin, it was possible to identify nineteen whose practice ranged from Highbury to Chelsea. This surely establishes the endemicity of the disease.

Symptoms and physical signs of fifty-three patients with 'epidemic neuromyasthenia'

Symptoms and physical signs in terms of percentage incidence are shown in Figs 1 and 2. Headache was the most frequent symptom; sometimes both frontal and occipital and accentuated by movement. Acute vertigo was the presenting feature of five cases; in others it occurred intermittently in the

FIG. 1. Proportions of group complaining of particular symptoms (53 patients).

*Tremor; twitching; spasm; cogwheeling; fasciculation.

FIG. 2. Proportions of group displaying particular physical signs (53 patients).

course of the illness. A combination of headache, dizziness, nausea, vomiting and extreme lassitude was common. Some patients complained of a sense of 'deadness' in a limb. Muscle cramps, twitchings and extreme muscle tenderness were common. Visual phenomena generally took the form of blurring of vision but diplopia was not infrequent. 'Paresis' occurred in 67% of cases. This is not a satisfactory term as the weakness is the result of an unusual form of muscular fatigability which is the predominant clinical feature of the disease. Lymphadenopathy affecting chiefly the cervical glands, and exaggerated tendon reflexes were found in at least 50% of cases. Sensory impairment generally presented as areas of hyperaesthesia (often corresponding with the distribution of deep muscle tenderness) interspersed with patches of hypoalgesia. Acute myalgia was present in 40-50% of cases. This was sometimes obvious as the patient winced even on light palpation of the affected muscle; but much more frequently it took the form of minute foci of muscle tenderness which had to be carefully sought and for no ostensible reason were generally found in the trapezii and gastrocnemii. Muscle involvement sometimes took the form of severe and painful spasm, tremor, twitchings, cogwheeling or fasciculation. Extensor plantar responses were found in 16% of cases and in two instances persisted after discharge from hospital. Cranial nerve palsies were present in just under 10% of cases, the third, fifth, seventh and eighth nerves being chiefly affected.

Evidence of involvement of the sympathetic nervous system or actual hypothalamic damage was to be found in most cases. This often took the form of orthostatic tachycardia (which Leon-Sótomayor (1969) states does not occur in cases of hysteria), chilliness of the extremities with increased sensitivity to cold, circulatory impairment and hypothermia.

Showers of petechiae or larger ecchymotic areas on the extremities, severe sweating, constipation, bladder disturbances often so insistent as seriously to interfere with sleep, and the appearance of an area of ghastly pallor around the mouth or of the whole face (usually noticed by friends or relatives some 20-30 min before the patient complained of feeling ill) were frequent events.

Virological and serological investigations were negative. Blood counts were done in all cases and showed the leucopenia which is consistent with virus infection. There was no anaemia. The ESR was normal or only slightly raised. Electromyography was carried out in twenty-five cases and was abnormal in twelve. The temperature was generally little raised but in one case reached 39.2° C and was maintained at a level of 38.8° C for 5 days.

'Epidemic neuromyasthenia' in North Finchley, London, in 1964-1967

Important new features of the disease were encountered in an outbreak in a circumscribed area of North Finchley between 1964 and 1967. These cases were seen at a much later stage of the disease and after the initial illness was long passed. An opinion was sought on account of persistence of fatigue, impairment of memory and inability to concentrate. The muscular fatigability was striking; while in some cases it persisted throughout the day, in others it abated after a good rest only to return following a short period of activity. It was very noticeable that no cases occurred among sedentary people and this might afford an explanation for the absence of the disease among the patients in the Royal Free Hospital, or among the community of nuns who shared a building with a teaching college in Newcastle (1959). The attack rate among 120 student teachers was 40% whereas there was only one case among the nuns engaged in cooking or teaching in the college.

Unilateral weakness of the masseter muscle was noted in many cases but otherwise no evidence was found of cranial nerve palsies or nystagmus. A combination of hypothermia, hypoglycaemia, polydipsia and the characteristic fatigability was common. Temperatures as low as 34.5° C were registered. Three patients became unconscious; one was known to be prone to attacks of hypoglycaemia; the second had no recollection of being taken to hospital while the third did not remember travelling in a car and falling out of it on opening the door. All recovered with the administration of glucose.

Mental changes in 'epidemic neuromyasthenia'

Mental changes were a feature of a considerable number of cases. Emotional lability and impairment of both memory and concentration were common.

Vivid and terrifying nightmares were often reported. There were sometimes marked changes in personality. Many patients over-elaborated the recital of their symptoms and this was associated with impairment of judgement and/or insight. Mental as well as physical exhaustion could be severe. When the hypothesis of 'mass hysteria' was put forward by McEvedy and Beard (1970), Compston *et al.* (1970) reported that they had seriously considered a diagnosis of hysteria but the occurrence of low grade fever in 89%, of lymphadenopathy in 79%, of ocular palsies in 43% and of facial palsy in 19% of patients rendered it untenable. Acheson (1954) for similar reasons rejected the hypothesis in respect of the fourteen cases he had earlier reported among the staff of the Middlesex Hospital.

Two doctor patients described transient speech difficulties both in their initial illness and later in relapses. They found they were using a different word (for example 'good' when they meant 'bad') from that which they intended. Kendell (1967) has described in detail the case histories of two nurses aged 19 and 24 years. Both had bad psychiatric histories, and hysterical features were prominent in both their illnesses. But both had abnormal electromyograms and in one case paresis was unaffected by hypnosis and remained unchanged for 12 years while other symptoms disappeared. He had no hesitation in diagnosing both cases as instances of 'benign myalgic encephalomyelitis' and concluded with a most prophetic statement, 'the issue is important because other young women have been, and will continue to be, diagnosed as hysterical under similar circumstances with the resulting risk of their treatment being misdirected and their doctors' attitudes to them altered in unhelpful ways'. That is precisely what subsequently happened. Very many patients, however, have shown no evidence of mental instability, and have come to terms with the limitations which the disease imposes on them although this may sometimes necessitate giving up their occupations. As a result of the widespread impression that they are 'neurotic' some have received scant sympathy or understanding from their doctors.

Muscular fatigability

Abnormal muscular fatigability is the dominant clinical feature of the disease. It has been suggested by Dr David Wilkie that this phenomenon might result from damage to mitochondria. Parish (1974) also considered that 'there is a prolonged metabolic disorder in many patients which may be affecting cellular energy systems and antibody production'.

Dr Wilkie advocated a series of biochemical investigations that might provide a useful source of information and Dr Alan Rundle of St Lawrence's

Hospital, Caterham, has kindly examined blood from seven patients with unequivocal 'epidemic neuromyasthenia'. He has estimated the serum levels in units per litre of creatinine phosphokinase, lactic dehydrogenase, glutamic oxalo-acetic transaminase, glutamic pyruvate transaminase and γ -glutamyl transpeptidase.

All seven patients produced pathologically high levels of lactic dehydrogenase and glutamic oxalo-acetic transaminase. The full details of these studies will be reported later as they clearly indicate metabolic disturbance.

Late results

A limited follow-up study has been carried out which suggests that the aftermath of this disease falls into three categories:

(1) Those who recover completely or nearly so. This includes a senior physician in a London teaching hospital who could regard herself as restored to normal health only after 10 years. It also includes a senior member of the nursing staff who has also recovered but with some weakness of the intercostal muscles. It further includes a very large number of patients who find that they are unable to perform some hitherto simple manoeuvre such as peeling potatoes or inserting a key into a lock without considerable difficulty.

(2) Those who recover but are prone to relapse. These are not infrequent and do not necessarily repeat the pattern of the original attack. Excessive physical fatigue would certainly seem to be the factor that triggers a relapse. This may occur suddenly when the patient feels he or she has almost recovered; alternatively there may be long intervals between episodes and as long as 4 years has been recorded.

(3) Those who show no recovery at all. These certainly include many who are not in a position to get adequate rest periods. They are compelled to accept the limitations which the disease imposes on them and often do so in a remarkably courageous way. The advice that is often given to 'snap out of it' is totally misplaced and wrong. Adequate rest periods are the only way in which some degree of improvement can be assured. A patient should always be given encouragement and hope that this may be achieved.

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Discussion

DR W. C. MARSHALL (London): Has it ever been observed in a woman during pregnancy?

DR A. M. RAMSAY: I have not observed it in a woman during pregnancy not have I seen any menstrual disturbance in these cases.

DR R. GREENBERG (London): In how many cases have you seen bulbar signs, particularly difficulty in swallowing, or weakness of the palate?

DR A. M. RAMSAY: I have not seen any though some such were observed at the Royal Free Hospital.