Myalgic encephalomyelitis—report of an epidemic

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SUMMARY. The relationship between the group B Coxsackieviruses and a wide variety of illnesses, particularly pleurodynia and myo/pericarditis, is already well established. The detection of raised levels of neutralizing antibody to these viruses in a group of patients in a rural practice presenting with an illness resembling myalgic encephalomyelitis (ME) was therefore unexpected. This is a most distressing and debilitating illness for the patient and the affected family. What is the immunological failure in these patients which apparently allows this virus to persist causing such unusual and bizarre illness? At present ME is probably much commoner than is realized, the majority of patients being given the dismissive diagnosis of psychoneurosis.

Introduction

DURING the period from January 1980 to June 1981, several patients in a rural practice in Ayrshire were affected by a curious illness. The symptoms were so protean that, had only one or two patients attended surgery, the nature of the illness might have been overlooked. The clinical features bore a striking resemblance to those of previously described outbreaks of an illness which has gone under a number of designations—epidemic vegetative neuritis,[1] persistent myalgia following sore throat,[2] benign myalgic encephalomyelitis,[3] epidemic neuromyasthenia,[4] Royal Free disease,[5] Iceland disease[6] and epidemic myalgic encephalomyelitis.[7] The last term seems to encompass the most important features of those epidemics. It must also be mentioned that the illness may occur in sporadic form.[8]

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Table 1. Twenty-two patients with suspected myalgic encephalomyelitis (ME).

Total number of patients	Age range (years)	Number of patients with elevated Coxsackie B titres	
		⩾512	256
16 female	8–53	11	1
6 male	10–41	2	4

The outbreak described here has an important feature in that many of the affected patients were found to have raised neutralizing antibody titres to group B Coxsackieviruses.

By reporting the clinical features of this epidemic we hope to alert other general practitioners to early recognition of myalgic encephalomyelitis (ME) and thus help future studies.

Clinical features

During the study period a total of 22 patients with suspected myalgic encephalomyelitis were seen. Sixteen were females aged between 8 and 53 years and six were males aged between 10 and 41 years (Table 1). The disease appeared either as an acute or a subacute illness. The acute symptoms took many forms but brainstem signs were common. These consisted of vertigo, hyperacusis and tinnitus. Other patients complained of chest pains on exertion, often with palpitations. Some patients developed an acute anxiety state, often accompanied by depression, while in a few there was a reversal of the sleep pattern with early morning wakening. Patients who had a subacute onset often noticed increasing anxiety, depression without a cause, muscle pains and aches, coarse muscular twitchings and odd paraesthesiae. Once the disease was established, the most characteristic symptom was extreme exhaustion, particularly after exercise. This exhaustion was also noticeable after any degree of emotional or mental strain; it was the most characteristic feature of the

Table 2. Main systems involved in 22 cases of suspected myalgic encephalomyelitis. In 67 per cent of cases there was a relapsing course.

System involved	Percentage of cases
Psychological symptoms	100
Musculoskeletal	80
Central nervous	75
Gastrointestinal	65
Cardiovascular	45

illness and the other symptoms appeared to be of secondary importance.

Case report

A 41-year-old airline steward presented in August 1980 with upper chest pain and exhaustion; these symptoms had been precipitated by a bicycle ride. The initial diagnosis was myocardial ischaemia. Further questioning elicited the following additional symptoms: curious feelings of panic at work with no specific provocation; increased anxiety and irritability, sleep disturbance with early morning wakening, fine 'true' vertigo, night sweats, pains in arms and legs, diarrhoea. All tests including electroencephalography were normal. Coxsackie neutralizing antibody titre = 1024 (B2).

Several weeks later his eight-year-old daughter became unwell. The symptoms were those of exhaustion with rapid fatigue on exercise. She had vague muscle pains and felt dizzy; diarrhoea was also present. She began to fall asleep in class, and attendance at school thus became impossible. Coxsackie neutralizing antibody titre = 1024 (B1, B4). Convalescence was prolonged.

The remaining members of the family—his wife and young son—were apparently unaffected.

Some patients reported that alcohol aggravated their symptoms while others found that caffeine-containing products increased their fatigue. One patient and the wife of another patient became pregnant; both pregnancies were uneventful apart from extreme fatigue in the ME case. The major symptoms in the affected patients are shown in Table 2.

Results of routine laboratory tests were normal. Virological studies, however, revealed that 18 (82 per cent) of the 22 patients had elevated neutralizing antibody titres to Coxsackie B. Of the 16 female patients, 11 (69 per cent) had titres ≥ 512 and one (6 per cent) had a titre of 256. The corresponding figures for the six male patients were two (33 per cent) with titres ≥ 512 and four (67 per cent) of 256 respectively. Titres of less than 256 are not normally regarded as significant.[9] Twelve of the 18 Coxsackie B 'positive' patients had symptoms which persisted for at least 6 months (Table 3).

Treatment consisted of supportive care; benzodiazepines were of help as was carbamazepine (Tegretol) 100 mg tds in reducing the severe muscle aches. Pizotifen (Sanomigran) relieved the headache and improved the appetite where weight loss was prominent. No treatment was given for diarrhoea or arrhythmia. Home help and district nursing services were needed for several patients. Since June 1981 no further cases of myalgic encephalomyelitis have been seen in this practice.

Table 3. Details of patients with raised neutralizing antibody titres to Coxsackie B virus.

Case number	Age of patient (years)	Sex	Onset of ME	Symptoms persisting >6 months	Highest Cox B titre recorded
1	52	F	1978	Yes	256 (B4)
2	53	F	Jan 1979	No	512 (B3)
3	30	F	Aug 1979	Yes	1024 (B2)
4	36	F	1980	Yes	512 (B1)
5	34	M	Jan 1980	Yes	512 (B1)
6	36	F	Jan 1980	Yes	1024 (B4)
7*	33	M	Feb 1980	Yes	256 (B3)
8	33	M	Mar 1980	No	256 (B2,B4)
9**	41	M	Aug 1980	Yes	1024 (B2)
10	40	M	Aug 1980	No	256 (B1,B3)
11	36	F	Sep 1980	No	512 (B4)
12**	8	F	Oct 1980	Yes	1024 (B1,B4)
13	33	F	Oct 1980	No	1024 (B2)
14	32	F	Oct 1980	No	1024 (B4)
15*	34	F	Nov 1980	Yes	1024 (B2,B4)
16***	35	F	Jan 1981	Yes	1024 (B4)
17	10	M	Apr 1981	Yes	256 (B2)
18	39	F	May 1981	Yes	1024 (B4)

*The patients in cases 7 and 15 were mother and father of girl who had onset of ME in Sept 1980 (Cox B1 titre of 128).

**The patients in cases 9 and 12 were father and daughter. Mother (Cox B1, B3 titres of 128) successfully delivered normal baby Dec 1980.

***The patient in case 16 successfully delivered normal baby Jan 1981.

Discussion

It was the large number of similarly affected patients in this practice, comprising 4,500 patients, that drew our attention to this condition. Clearly, if only one or two patients had presented with these symptoms they could well have been regarded as neurotic, depressed or hypochondriacal. Indeed, several of our patients were referred initially for a psychiatric opinion. Exhaustion and headaches are perhaps the two commonest symptoms met with in general practice, and when full physical examination is normal and there are no abnormal laboratory findings treatment is usually empirical and difficult. The unusually large number of patients presenting, within a short period, with symptoms of extreme exhaustion and psychological upset, and the fact that they were all known to have good pre-morbid personalities, made us consider an organic cause for their illness.

The dilemma of whether or not such patients do have an organic illness has been the stumbling block in the diagnosis of the many previous outbreaks of similar illness. It was the lack of abnormal laboratory findings and the failure to demonstrate persistent physical or

Table 4. Laboratory findings reported in cases of myalgic encephalomyelitis.

Urine
Creatinuria
Peripheral blood
Lymphocytosis; Abnormal lymphocytes
Serum
Increased lactic dehydrogenase, glutamic oxaloacetic transaminase concentrations; Positive anticomplementary activity
Cerebrospinal fluid
Rarely, increased cells and protein, and a positive Pandy test
Electromyography
Reduced motor unit potentials on volition
Electroencephalography
Minor non-specific changes

neurological deficits that led McEvedy and Beard[10] to suggest that these patients were hysterical. However, close scrutiny of the literature reveals that a number of subtle but definite abnormalities have been recorded in previous outbreaks; some of these are listed in Table 4. Jaundice and lymphadenopathy have been described. Muscle twitchings, fasciculations, transient pareses, muscle tenderness and meningism have also been recorded.[11] These clinical findings have often been transient and are unfortunately rare. Laboratory tests have found creatinuria, lymphocytosis, increased serum enzymes, and abnormal electromyographic features.[5,12] Previous virological studies have been unrewarding except that in one outbreak similar symptoms, including general malaise, lymphadenopathy and occasional meningitis, were found to be associated with infection with Echo 9 virus,[13] now better known as Coxsackievirus A23.

The significance of elevated neutralizing antibody titres to Coxsackie B viruses in our patients is unknown. Certainly Coxsackie B viruses have been identified previously in the epidemics of myalgia known as Bornholm disease.[14] In the 1965 Coxsackie B5 outbreak in the United Kingdom and Europe both the cardiovascular and central nervous systems were involved.[15] These viruses demonstrate a characteristic myotropism since group A and group B Coxsackieviruses have also been cited as causing chronic polymyositis and have been isolated from the muscle of infants and adults with myositis.[16,17]

In our series of ME cases, interpretation of the high static Coxsackie B antibody titres seen is extremely difficult. Previous studies[9,18] suggest that the higher the titre observed the greater is the probability of recent infection. Nine hundred and fifty normal adults in the west of Scotland have been tested for presence of Coxsackie B neutralizing antibody; titres ≥ 512 were detected in only 4 per cent of this sample and titres of 256 in 10 per cent.[19] In our ME patients the corresponding figures were 59 per cent (≥ 512) and 55 per cent (256). It seems reasonable to conclude that we have observed a real difference in the Coxsackie B antibody status between our ME patients and our normal adult population.

Current research suggests that there are subtle but definite immunological abnormalities in patients with myalgic encephalomyelitis[12,20] and that these abnormalities may represent the presence of a persistent virus. Documentation and study of further outbreaks of this illness may help to elucidate its cause.

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