Coxsackie B infection in a Scottish general practice

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SUMMARY. The authors describe 38 cases of protracted illness, characterized by varied multisystem symptomatology. Significant antibody titres to Coxsackie B viruses, suggesting recent infection, were found in these 38 patients (47 per cent of 81 cases investigated). The syndrome has many of the features of myalgic encephalomyelitis (ME), a condition which has frequently been found in closely clustered epidemics but seldom in sporadic or endemic form. The reported cases emerged over a four-year period and fresh cases continue to appear.

Introduction

FOUR years ago we began to recognize a chronic and debilitating illness affecting mainly young, healthy adults. Striking features were multisystem symptoms and fluctuating course of relapse and remission, generally leading to a gradual resolution over many months or even several years. Significant titres of neutralizing antibody to Coxsackie B group viruses were detected in the serum of some patients, and we noticed an association between this syndrome and serological evidence of recent infection by these viruses.

The illness itself is similar to myalgic encephalomyelitis (ME), which was reviewed comprehensively by Behan,[1] and which has been closely linked with Coxsackie B infections in two recent reports from Scottish general practices. Fegan and colleagues' description of 18 cases suggested a fairly clear-cut epidemic with a number of instances of close contact spread.[2] Keighley and Bell[3] examined serum from 20 patients with ill-defined chronic illness and found elevated antibody titres to Coxsackie B viruses in 16 cases, of which 13 were eventually thought to be ME; these cases occurred in an apparently sporadic pattern, without obvious connection between patients. In another study in the West of Scotland, 1,000 adults were screened for Coxsackie B antibodies and 10 per cent were found to have titres ≥ 256 and 4 per cent ≥ 512.[4]

We decided to look for evidence of Coxsackie B infection in patients with the ill-defined symptoms described above.

Patients and methods

The practice of 9,500 patients covers half the population of Helensburgh, a small seaside town on the Firth of Clyde. Many of these patients are Glasgow commuters and many others are employed at two local defence establishments. A large number of Royal Navy personnel live in the area, and the practice is responsible for the care of their families although not of the servicemen themselves.

Between 1978 and August 1983, investigations were carried out in 81 cases of suspected Coxsackie B infection. The serological tests were performed at the Regional Virus Laboratory at Ruchill Hospital, Glasgow.

Results

The results of serological tests in suspected cases of Coxsackie B infection after 1978, when an isolated case occurred, are shown in Table 1. Eighteen of the 38 positive cases were confirmed in the first six months of 1983. Thirty-eight (47 per cent) of the 81 patients

Table 1. Results of serological tests in suspect cases after 1978 (when one isolated case of Coxsackie B infection was found).

Year	Positive	Negative
1979	Nil	Nil
1980	3	5
1981	9	12
1982	7	12
1983 (to August)	18	14

examined were found to have significantly raised titres (>256). Details of the 38 patients with raised Coxsackie B antibody titres are listed in Table 2. Six other patients had borderline titres of 128 to serotypes B1, B3 and B5, but it was not clear whether these cases belonged to the positive group or not. Antibodies to a variety of Coxsackie B serotypes were found, of which B4 was the commonest (25 cases). However, we were unable to show a clear relationship between any particular serotype and specific symptom complexes. We failed to demonstrate any rising antibody titres, suggesting that infection was well established before the investigation.

Table 2. Details of patients with raised Coxsackie B antibody titres (arranged in ascending order of antibody levels).

Case no.	Age (years)	Sex	Symptoms*	Highest antibody titre	Serotype	Additional features†
1	32	F	ABC	256	B4	
2	31	M	AB	256	B4	Z
3	38	F	B	256/256	B3 B4	Y
4	35	F	BDF	256	B4	
5	31	F	ABF	256	B4	XY
6	33	M	AB	256	B2	
7	46	F	AB	256/128/256	B1 B3 B4	
8	38	M	BD	256	B2	Z
9	45	F	BE	256	B4	
10	29	M	ABCG	256	B3	
11	43	M	B	256	B2	
12	32	M	ABC	256/256	B2 B3	
13	19	F	ABCFG	256	B4	
14	38	F	ABC	256	B2	
15	56	M	ABF	256	B2	Y
16	31	F	AG	256	B4	
17	20	F	ABCDE	128/256	B2 B4	
18	37	F	ACE	256	B4	
19	62	M	A	256/256	B2 B3	Z
20	31	F	ABCE	256/256	B3 B4	
21	36	F	AB	512	B4	
22	29	F	CEG	512	B3	XY
23	33	M	ABC	512	B4	Z
24	22	F	CG	512/256	B3 B4	Z
25	40	M	ABD	256/512	B3 B4	
26	67	F	ADF	512	B2	Y, died of Ca pancreas
27	30	M	ABF	512/128	B2 B4	
28	36	F	ABEF	512/256	B2 B4	Y
29	36	F	ABF	512	B2	
30	37	F	BDE	512/256	B1 B3	
31	24	F	C	512	B4	
32	59	M	BF	512	B4	
33	45	M	B	>1024	B2	
34	35	F	BEF	>1024	B4	X
35	26	F	A	>1024	B4	Z
36	38	F	ACG	>1024	B4	
37	41	F	ABDEF	>1024/512	B2 B4	
38	24	F	E	>1024/512	B2 B4	

*A = General symptoms: malaise, sweating, lightheadedness, headaches.
B = Cardiovascular: palpitations, chest pain, dyspnoea.
C = Musculoskeletal: myalgia.
D = Vestibular: vertigo, dizziness.
E = Psychiatric: depression, anxiety, poor concentration.
F = Gastrointestinal: anorexia, vomiting, diarrhoea.
G = Neurological: paraesthesia, cranial nerve palsy, slurring of speech.

†X = Onset within six months of parturition.
Y = Significant past psychiatric history.
Z = Required hospital admission.

Classification of symptoms, many of which were 'non-specific', was difficult. Despite some overlap, the 38 patients can be divided into two groups on the basis of different symptoms:

1. A 'cardiac' group in which palpitations were the commonest feature (24 patients);

2. A smaller but more severely ill 'neurological' group (six patients).

More vague symptoms, such as malaise, were common to both groups.

Typically, healthy adults in their thirties were involved, but the age span was 18 to 67 years with a mean age of 36.7 years. The female to male ratio was 25:13.

Case reports

Two representative cases are described.

Case 24

A previously well, fit and healthy 22-year-old schoolteacher presented in December 1980 with a two-day history of tingling and numbness, patchy in distribution but mainly involving the left side of her body, with headache, and pain and tingling in the distribution of the maxillary division of the right trigeminal nerve. She described feelings of panic and apprehension in the first few days of the illness.

She developed vertigo and complained of tightness around her chest and throat, pain in her left ear and difficulty in opening her mouth. Further discomfort developed in the joints of both hands, particularly on the right side, and recurrent headache became a problem.

Investigations included full blood count, erythrocyte sedimentation rate (ESR) and blood film, liver function tests, plasma electrolyte and serum protein assays. All tests were normal, as was cerebrospinal fluid (CSF) examination. Radiographs of teeth, sinuses and chest were normal. Brain scan was normal, but electroencephalography (EEG) showed evidence of bilateral disturbance. Her serum showed Coxsackie B titres of B3 512/512 and B4 256/256, suggestive of recent infection. Repeat EEG eight weeks later showed continuing bilateral abnormalities.

She continued to have joint and facial pain and developed intermittent disturbances involving zigzag lines and patchy scotomata. Her progress has been slow, with several weeks off work in the initial stages, followed by frequent relapses lasting one or two weeks, slowly becoming less intense and less frequent. During these relapses she can experience any of the symptoms already described as occurring in the initial episode, and she is frequently miserable during these periods.

In February 1982 she developed symptoms of loss of concentration, early morning wakening, irritability and anorexia, all of which persisted. These symptoms responded to eight weeks treatment with dothiepin hydrochloride. Her relapses are now occurring every two months or so, but she is still a long way from the fit, active young woman that she was before December 1980.

Case 33

A fit, healthy 45-year-old man with no previous medical history presented in December 1980 with feelings of fullness in his upper abdomen, increased awareness of his heartbeat and dropped beats. He was apprehensive and feared for his life during the episodes of palpitation. He had been feeling generally unwell for several days before presentation and had been noticing increasing shortness of breath on exertion. His Coxsackie titres were >1,024 to serotype B2, suggestive of recent B2 infection. Atenolol 100 mg per day settled his cardiac symptoms to a great extent, but we were only able to discontinue treatment after 14 months. Since then, his exercise tolerance has slowly improved, but he still has bouts of palpitation and unfitness from time to time, usually more pronounced when he is fatigued from other causes.

Treatment

These patients have a high morbidity and a high consultation rate. In 15 cases beta-adrenergic blocking agents were used for troublesome palpitations and a marked reduction in symptoms was experienced. These drugs seemed to give some relief from the feelings of panic and impending death described by many patients, so perhaps these distressing features were due to the cardiac abnormality. Minor tranquillizers were also used in small doses to help the anxiety symptoms which commonly occurred. Frequent reassurance and support are required over long periods, symptoms persisting for several years in some cases.

Discussion

Our findings suggest a relationship between Coxsackie B infection and the illness described. Positive serology was found in selected cases far in excess of the expected rate for the population. The results confirm the findings of Keighley and Bell,[3] who described the situation in a rural practice 30 miles from our own; neither group was aware of the activities of the other until recently.

The possibility of Coxsackie B infection was suspected in a number of patients who posed diagnostic difficulties, and these accounted for some of the seronegative results. Eight of these patients had past psychiatric histories which could have accounted for their continuing vague symptoms. In several other seronegative cases definite diagnoses of quite different kinds were subsequently made. These included cerebral neoplasm, multiple sclerosis, cardiomyopathy and rheumatic heart disease. (Coxsackie B viruses have been associated with heart disease.)[5]

The female to male ratio was similar to previous findings.[1] We have not seen any patients under the age of 18 years in whom we suspected this illness. There have been no obvious connections between the cases, but we have noted a marked socioeconomic class bias. There have been many more cases in social classes I and II than would be expected if distribution by social class were random. Only seven of the 38 patients live in local authority housing, the remainder being owner-occupiers. Another striking feature was the dearth of cases involving families of Royal Navy personnel: we found only three cases, despite the fact that this group comprises one third of our practice. Probably because of our increased awareness of the syndrome, we continue to find new cases and there is no sign of a fall in incidence.

Previous reports have generally dealt with discrete epidemics rather than the 'sporadic' or 'endemic' pattern which we have found. We have no evidence to suggest a seasonal variation either in date of onset or date of presentation, nor do we have any evidence that the infection was acquired outside our local area or abroad. We believe that the diagnosis is frequently being overlooked in both hospital and general practice, and that a label of psychoneurosis is erroneously applied in many cases. Even in the absence of specific treatment, we have found that patients and their relatives gain relief from the discovery of an organic diagnosis in these situations.

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Ambulatory ECGs and 'funny turns'

Episodic diffuse cerebral symptoms and unexpected falls were investigated by ambulatory electrocardiography in nine men and 19 women aged 65 years or more. Eight subjects with episodic dizziness or syncope had cardiac arrhythmias which are known to be capable of causing these symptoms, and four of these had symptoms at the time of the arrhythmia. However, only one case was detected by ambulatory electrocardiography alone. No significant arrhythmias were found in any of the remaining subjects. When 17 symptomatic subjects were compared with 17 age- and sex-matched asymptomatic controls, cardiac arrhythmias known to be capable of causing symptoms were commoner in the symptomatic group, but the differences were not statistically significant. Ambulatory electrocardiography is of no more value than standard electrocardiography in the detection of arrhythmias associated with diffuse cerebral symptoms in elderly people.

Source: Taylor IC, Stout RW. Is ambulatory electrocardiography a useful investigation in elderly people with 'funny turns'? *Age Ageing* 1983; **12:** 211-216.