'Epidemic neuromyasthenia' in Southwest Ireland

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Summary

During the course of an obscure illness in a teenage girl it was eventually realized that the diagnosis was 'epidemic neuromyasthenia'. The illness which occurred between February and September 1976 was characterized by fatigue, pallor, headache, nuchal pain, alterations in mentation, dizziness, nausea and vomiting, paraesthesiae, weakness and heaviness of limbs, and a prolonged relapsing course. Investigation brought to light fourteen patients with similar symptoms - twelve female and two male. In view of the shortcomings of retrospective enquiries, especially those involving the assessment of notes made by other people, and the problem of trying to define a non-fatal illness with protean symptoms, many of a non-specific nature, with few physical findings and negative laboratory studies, caution is necessary. Under these circumstances it is claimed on clinical epidemiological evidence that a diagnosis of 'epidemic neuromyasthenia' could be sustained confidently in three patients and probably in a fourth. Six patients were considered possible cases and four were rejected.

Introduction

This author's task differs somewhat from the preceding contributors. He is not a practising physician and did not examine any of the patients mentioned in this report. Rather he is an epidemiologist who, because of personal involvement, persistence and the help of others, realized, at the end of an outbreak of an obscure illness, what the condition was.

The illness which occurred in Southwest Ireland between February and September, 1976, was characterized principally by fatigue, pallor, headache, neck pain, alterations in mentation, dizziness, nausea and vomiting, paraesthesiae, weakness and heaviness of limbs and a prolonged relapsing course.

The author is cognisant of the shortcomings of retrospective enquiries especially those involving the assessment of case notes made by other people. A further complication is the problem of trying to define a non-fatal illness with protean symptoms, many of a non-specific nature, with very few physical

findings and generally negative laboratory studies. However, a diagnostic group is perceived to exist when a particular combination of symptoms and signs occurs together more frequently than would be expected by chance and the combination can be understood or explained in the context of the present level of knowledge in the medical sciences (Lowe and Lwanga, 1978). On the basis of probability he submits that the clinical and epidemiological evidence presented here corresponds with descriptions of 'epidemic neuromyasthenia' which have occurred elsewhere.

Index case

A 16-year-old schoolgirl awoke on May 26th 1976 with cramp in the calf muscles of one leg. On rising she said she could not see properly and everything was spinning. Having returned from the bathroom she fainted. She was very pale and complained of headache. However, she went to school and also the following day but had to be brought home because of the headache. After three further days of observation during which her temperature did not exceed 37.5°C (99.5°F) she was admitted to the Bon Secours Hospital, Cork, on May 30th because of a worsening headache. At this stage she complained of marked dizziness, weakness and inability to walk because of loss of balance. Next day she had a lumbar puncture. Her CSF was normal and her temperature settled after 4-5 days. She was discharged on June 7th feeling fairly well and with a presumptive diagnosis of a viral infection. On June 16th she went back to school but the headache recurred and she had to take to her bed where she stayed with persistent headache and a temperature which never exceeded 37.8°C (100°F). In July, an enquiry was made of the Public Health Laboratory Service at Colindale to know if there was any unusual virus epidemic in the United Kingdom. On August 18th the patient was readmitted to hospital for further investigations. All of these (Table 1) which were carried out from May to August were negative or normal with the exception of a relative lymphocytosis once (WBC $5.0 \times 10^9/l$, 42% lymphocytes).

Electron microscopy of faeces (late) did not show any virus particles. The serum antibody titres of the index case are presented in Table 2. She was discharged on August 29th. The diagnosis appeared to

TABLE 1. Investigations normal or negative in index case

Haemoglobin, ESR, Blood culture
Blood count (relative lymphocytosis once)
Iron binding capacity, Percentage saturation
Urine, Faeces, CSF
Sodium, Potassium, Chloride, Proteins
Bilirubin, Thymol Turbidity, SGOT
Alkaline Phosphatase, CPK
Blood urea, Plasma lactate
Paul Bunnell, Q fever, CMV, Anti-streptolysin O
Leptospirosis, <i>Mycoplasma</i> , Toxoplasmosis, Brucellosis,
Tuberculin, Complement studies, Protein electrophoretic
pattern
X-Rays of: chest, skull, sinuses, cervical spine

TABLE 2. Serum antibody titres of index case

Sub-acute myelo-optic neuropathy (SMON)	1/120
Repeat SMON	1/56
Herpes simplex virus, cytomegalovirus, adenovirus	< 1/8
Epstein-Barr virus	negative
Measles	1/32

be a persistent viraemia or vestibular neuronitis. Further letters to the Public Health Laboratory Service, Colindale, elicited a suggestion that the condition might be something akin to Royal Free disease. The ideas of McEvedy and Beard (1970) concerning the latter disease generally prevail among those who have not seen cases of 'epidemic neuromyasthenia' but on reading Acheson's (1959) review article the author was convinced that the description of benign myalgic encephalomyelitis or epidemic neuromyasthenia aptly described the index case's illness.

Response to circulars

It was now September and all physicians and general practitioners in the local health board area of Cork and Kerry were sent a circular informing them that over the previous year or so there had been an epidemic, locally if not nationally, of an unusual illness which in retrospect appeared to be benign myalgic encephalomyelitis. The main symptoms were listed and a plea was made to be informed of cases fitting the general description of the illness. Of note were the following:

(1) A report from a doctor in Tralee (70 miles from Cork) who said he had seen at least five or six cases recently in his area, two of whom were admitted with meningitis.

(2) A report from a general practitioner in Cork city quoted in full 'I have seen about twenty cases

which you have described in your letter of 15th September. Four were healthy male senior school children and young adults, the remainder were females up to 30 years of age. All had temperature 100° F, pulse about 100/min. Nystagmus was a prominent feature. Some collapsed with vertigo. Cramps and muscular weakness were common. None of my patients had paresis but one has an abnormal EEG at present and he had diplopia at the onset. All had normal blood counts and ESRs. No patient was sent to hospital but treated with rest, drinks and observation, plus anti-emetics'.

(3) A general practitioner in North Cork who recalled seeing 'about a dozen cases that fit the bill' between May and July, mainly children.

(4) A physician from a contiguous area (Limerick) who said 'we have been observing these particular symptoms here quite frequently in the past 6 months but unfortunately we have kept no particular records about it or done any special investigations'. This letter should be read in conjunction with a report in the popular medical press which appeared in August (Report, 1976) and referring to the same area said 'the number of children admitted to hospital with viral meningitis has risen alarmingly from one or two cases a month, normal for this time of the year, to the present rate of four-five a week. Children from 2 to 14 years old are affected only the toddlers are exempt'.

(5) A letter from a general practitioner in Cork city who expressed her relief at getting the circular and said 'for the past 4 weeks I myself, have had all these symptoms, except photophobia. So miserable did I feel that I got the consultant to check out blood chemistry, etc. My main symptoms were blinding headache with nausea and dizziness, fever not higher than 100° F. The consultant was at a loss to explain these symptoms other than the inevitable psychosomatic'.

(6) A letter, from a doctor in Donegal (250 miles from Cork) following publication of a notice (Corridan, 1976), saying 'we have had an epidemic of, what is now in retrospect, myalgic encephalomyelitis, in this area during the summer months. Unfortunately we did not make a record of all the patients who had the illness, but two were sufficiently ill to warrant their admission to hospital. One was a nurse in the hospital'.

(7) *Reports of possible single cases from general practitioners.* There were eventually fourteen patients with a possible diagnosis of epidemic neuromyasthenia - two males and twelve females. Of the fourteen, one, a female teacher aged 46 years was excluded because on the weight of evidence it could reasonably be maintained that she had infectious mononucleosis (serum 1 year after start of illness - EBV antibodies IgG positive 1/128, IgM not

detected). Two other female teachers who had fifty and seventy lymphocytes respectively per $10^9/l$ in their CSF, with increased protein in one, were also outruled. The children of both women had diarrhoea and vomiting a few days before their mothers became ill. It is accepted that these women had viral meningitis. Another woman with a diffuse history and subjective complaints was also rejected for fear of making 'epidemic neuromyasthenia' a ragbag for patients without a definite diagnosis. There are therefore ten patients left, three of whom are claimed as cases of 'epidemic neuromyasthenia', one a probable case and six possible cases.

Case reports

To return to the index case, having been discharged from hospital the second time she was confined to bed at home with persistent headache, low grade temperature, photophobia, weakness, lethargy, pallor and other prominent autonomic nervous system symptoms. She had no inclination to read as she said she could not concentrate. In fact during September and October she was worse than at any other period since the start of the illness. About mid-November she began to feel somewhat better and in January, 1977, returned to school gradually although her headache and temperature persisted. She was back to normal by Christmas 1977. Reverting to the onset of her initial illness it is noteworthy that practically every day from the 18th to the 24th of that month she visited a patient in the paediatric ward of the Bon Secours Hospital.

Case 2

Opposite the index case in hospital was a 22-year-old nurse who was working in the maternity department of the same hospital. She had similar but more pronounced symptoms and was admitted the day before the index case. She became ill on 25th May with an influenza-like illness but carried on working. On the 29th May she felt dizzy and was sent downstairs for a cup of tea. On returning to work she could not climb the stairs because of the weakness of her legs and sat on the step. Eventually she finished work and as it was her half-day she went shopping in town. She collapsed there and can only remember finding herself in hospital. She says she could not see for 3–4 hr, felt weak, dizzy and had tremor in her left hand. She cried with headache, CSF normal, pupils equal and reacted to light, fundi normal. She had a relative lymphocytosis (40%); blood chemistry normal; bilateral extensor plantar responses, CNS otherwise normal; temperature for 3 days not greater than 38°C (100.2°F). She was discharged on June 17th still feeling very unwell. She improved gradually but in August developed severe tremor in both hands. She became difficult to live with and

emotional, cried easily and was excessively sensitive to people's enquiries as to how she was. On 10th November she had a very bad headache, plus chest and shoulder pain. She was readmitted to hospital and discharged after nine days. There was gradual improvement until she felt all right again by May, 1977. She is now well but complains of occasional dizziness and what she describes as 'rheumatism' of her left shoulder. When last examined her fundi showed bilateral temporal disc pallor with sharp cut edges.

Case 3

A 30-year-old nun working in the maternity department (same as case 2) of the Bon Secours Hospital, Cork, became ill on 21st February with a heavy head cold, went to bed and developed headache on 22nd February, pyrexial. Admitted to infirmary on 23rd February, cold improved but headache persisted. Returned to duty on 27th February although she still had headache. Next day (28th February) felt terribly weak and went back to bed. Readmitted to infirmary where she spent six weeks with headache, nausea, dizziness, hyperacusis and heaviness of legs. Her muscles felt weak, she developed a tremor of hands and could not read or study. She improved gradually and returned to work in June although she felt only about 75% right. Fully recovered by April, 1977 (yet people say she still has not recovered her normal pink cheeks). Relative lymphocytosis of 50% ($\text{WBC } 7.2 \times 10^9/l$).

Case 4

A nun aged 46 years from a geriatric hospital in Tralee was notified to the author by the nuns of the Bon Secours Hospital, Cork, as being a case of the same illness as the first three patients. She fell ill on February 27th in Dublin where she had been for 9–10 days. She had stayed overnight in the Bon Secours Hospital, Cork, on 13th February and visited the infirmary. In the geriatric home in Tralee in mid-February there was an epidemic of what was labelled influenza. It affected men and women, three patients died and three or four of the nuns were affected. It was a pyrexial illness with sore throat, pains in bones, remissions and relapses. The week before this patient became ill with severe headache and nausea she had several episodes of epistaxis. Her illness was characterized by great weakness and she wanted only to lie in bed. She was admitted to the Bon Secours Hospital, Tralee, and diagnosed as a virus infection. While there, she complained of chest pain, dizziness and photophobia in addition to her other symptoms. At one stage she had achromatopsia. She was referred to a Dublin hospital where she had a brain scan and lumbar puncture – both normal. She had a flat glucose tolerance curve but

was previously suspected of having hypoglycaemia and had been investigated for it. She was really not well all the year and had an exacerbation in December. In time, she made a gradual recovery.

Possible cases

Of the remaining six patients, two were male aged 19 years who are from the group of twenty or so cases seen by the general practitioner in Cork referred to earlier. The first had nystagmus, an EEG abnormality which had cleared when repeated 1 week later, temperature 38.9° C (102° F), exceptionally severe headache, weakness, pains in arms, legs and back, and hyperacusis. There was evidence of inco-ordination the day he became ill as he was inclined to strike an empty space when playing hurling and football. He had no lumbar puncture and gradually recovered over 3 months.

The second male started with diarrhoea, nausea and headache. He then developed neck pain and drowsiness. He complained of lack of power in his legs and had nystagmus. He recovered partially and went back to college. Four months after this he had recrudescence of the headache, neck pain and vomiting. His leg weakness also recurred and lasted 2 weeks. He claims that when he is under stress now his legs become weak and while generally well he is not quite the same as he was before the initial illness.

The third of the six was a 36-year-old married woman in Cashel (60 miles from Cork) who woke with pain in her left shoulder which got worse and spread to her occiput. This lasted for 1 week and the pain used to waken her at night. She developed nausea and vomiting and suffered loss of vision which lasted about 30 min. She could not walk from her bedroom to the bathroom because of the heaviness of her legs. An X-ray of the cervical spine was normal. She recovered after about one month. Since then her left shoulder feels weak.

The fourth case was a married woman aged 33 years who, when relaxed and having a drink, felt her arms becoming heavy. She became weaker the following days and thought she had influenza. After 2 weeks she consulted her doctor and a few days later was admitted to hospital complaining of headache, pain in her neck, shoulder, arms, chest and legs. Her eyes felt sore and she had a running nose. She did not have a lumbar puncture and was labelled a virus infection. On one occasion when she left her room she felt so weak she had to be brought back in a wheel-chair. She was discharged after 3 weeks still feeling weak. A month later she had nausea and vomiting. Shortly afterwards she went on holiday to North Africa and had not strength to swim. After another month she returned to full-time work gradually, the whole episode lasting about 4

months before she felt well again. Investigations including extensive complement studies were normal or negative with the exception of her urinary creatine : creatinine ratio which was reported abnormal.

The fifth case, a single woman aged 43 years was admitted to hospital in August complaining of numbness and tingling in her left hand and leg since February. These sensations lasted about 6 hr and occurred three or four times a week. She also had frequency of micturition. In hospital she had head and neck pain for a few days and fainted once; there was one minor temperature rise. She had bilateral extensor plantar responses, knee and ankle jerks were not elicited, CNS otherwise normal, lumbar puncture normal. All other investigations including glucose tolerance test normal. Symptoms still present but much less marked.

The sixth case was a 14-year-old girl who was brought to the author's attention in October 1977 following recovery from a recrudescence of symptoms which started in March 1976 when she fainted in school. At the time she had headache, feelings of hot and cold, numbness of shoulder, pain in rib cage, sore throat, formication, claustrophobia, nightmares, frequency of micturition and dysuria, malaise and could not stand because of weakness of legs. She also had photophobia, hyperacusis and dizziness. Her tonsillar glands were palpable. There was partial recovery over 6 weeks and she went back to school but could not concentrate. She slept during the day and had insomnia at night. She became very irritable and impatient, depressed, and wept readily. Symptoms recurred in March and September 1977. Investigations as an out-patient were negative except for a relative lymphocytosis (40%) in September 1977. Her doctor remarked on her pallor.

Electromyography was carried out about one year after the initial illness in the patient with infectious mononucleosis and showed a radicular neuropathy.

Discussion

There is no doubt in the author's mind that the index case and the nurse and nun in the Bon Secours Hospital, Cork, had 'epidemic neuromyasthenia'. The main difficulty lies in recognition of the condition (Graybill *et al.*, 1972). Accurate case delineation is difficult especially when unsupported by epidemiological evidence. Whether it is rare is conjectural but certainly in the absence of an epidemic must be very difficult to diagnose in an isolated instance. Fatigability, which is the most striking phenomenon in the clinical picture (Ramsay, 1976), was a marked feature of the Cork cases as was also a protracted course and relapsing nature. All observers commented on the pallor.

The significance of the subacute myelo-optic neuropathy (SMON) titre in the index case (performed by Dr Inoue in Kyoto, courtesy of the Public Health Laboratory Service, Colindale) is not known. She never had clioquinol in her life and the control had a similar titre. Regarding the probable case it would appear that the epidemic among patients and staff in Tralee was a genuine influenza but the condition which this nun had must have been different as she became ill in Dublin 9–10 days after leaving Tralee and is unlikely to have had the same condition as the patients. Because of doubt, however, she is considered a probable case of 'epidemic neuromyasthenia'.

There is no conclusive evidence that the twenty cases seen by the general practitioner in Cork and the cases claimed to have had 'epidemic neuromyasthenia' were of the same nature. Neither can one conclude that the increase in other parts of the country of cases of aseptic meningitis were related. Many of the possible cases could have had 'epidemic neuromyasthenia' but the diagnosis is reserved only for those who could not be claimed possibly to have some other condition. The significance of the abnormal creatine : creatinine ratio in one of the possible cases is not known because of difficulty in interpretation of the method used. The six possible cases are so considered either because of lack of sufficient investigation (only one had a lumbar puncture) or because of insufficient clinical and epidemiological evidence as strong as in the other patients.

No virus has definitely been incriminated as the cause of an epidemic although the illness has characteristics of such infection. Enteroviruses are suspected by some to be implicated. Their major target organs and site of major symptomatology are at a distance from their site of multiplication (Evans, 1976). The fact that most echoviruses are excreted for shorter periods than the other enteroviruses (Melnick, 1976a) and the virtual impossibility of detecting rises in antibody titre against all possible enteroviruses (Melnick, 1976b) complicate the situation. There may of course be more than one virus involved as different viruses can produce the same syndrome and the same virus can produce different syndromes.

In 1975 there was a preponderance of ECHO 19 isolations in England and Northern Ireland, which may have spread to the rest of Ireland later. The only isolation from the Republic of Ireland in 1976 was ECHO 19. In 1976 the predominant viruses (not in the CSF) found in patients aged 15 years and over with neurological symptoms, in England and

Northern Ireland were ECHO 30 and Coxsackie A9 and B5.

Innes (1970) theory might account for the failure to find a virus during an epidemic. He asked if it could be that enteroviral infection, in predisposed or previously sensitized subjects, sets in train some process, say of an allergic nature, which accounts for the similarity of symptoms and the chronic relapsing course. It may be relevant that one of the cases had a presumed viral infection when in primary school and ran a low grade temperature for a few months. Several children were affected. Also one of the possible cases was admitted to hospital as a query case of poliomyelitis and had a lumbar puncture when aged 7 years.

The Cork outbreak was unusual in that the index case occurred in the community and led to the discovery of other cases among nurses in the hospital to which she was admitted and where in fact she may have contracted the illness.

Acknowledgments

I thank the many doctors who replied to circulars and the following for their collaboration and access to patients Sr Aloysius, D. Atkins, P. Behan, D. Buckley, M. T. N. Callaghan, E. Dowsett, I. Drury, P. F. Duggan, S. Gardner, J. Gallagher, T. Gleeson, P. Gordon, E. Harrington, D. Kelleher, D. Loughnan, W. H. Lyle, V. McCarthy, A. McKenna, J. W. Magner, P. Michael, M. O'Shea, J. G. Parish, M. S. Pereira, W. Ryan, W. Shannon, G. Shorten. I also wish to thank Dr M. Thomas, and the editor of the Communicable Disease Report of the Public Health Laboratory Service, Colindale, for permission to quote from virus returns for 1975 and 1976.

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