

- 10 Hunter MS, O'Dea I, Britten N. Decision-making and hormone replacement therapy: a qualitative analysis. *Soc Sci Med* 1997;45:1541-8.
- 11 Porter M, Penney GC, Russell D, Russell E, Templeton A. A population based survey of women's experience of the menopause. *Br J Obstet Gynaecol* 1996;103:1025-8.
- 12 Kuh DJ, Hardy R, Wandsworth MEJ. Social and behavioural influences on the uptake of hormone replacement therapy among younger women. *Br J Obstet Gynaecol* 2000;107:731-9.
- 13 Abraham S, Perz J, Clarkson R, Llewellyn-Jones D. Australian women's perceptions of hormone replacement therapy over 10 years. *Maturitas* 1995;21:91-5.
- 14 Rymer J, Morris EP. Extracts from Clinical Evidence: menopausal symptoms. *BMJ* 2002;321:1516-9.
- 15 Eriksen PS, Rasmussen H. Low dose 17 β oestradiol vaginal tablets in the treatment of atrophic vaginitis: a double blind placebo controlled study. *Eur J Obstet Gynaecol Reprod Biol* 1992;44:137-44.
- 16 Zethraeus N, Johannesson M, Henriksson P, Strand RT. The impact of hormone replacement therapy on quality of life and willingness to pay. *Br J Obstet Gynaecol* 1999;104:1191-5.
- 17 Cooper C. Epidemiology and definition of osteoporosis. In: Compston JE, ed. *Osteoporosis: new perspectives on causes, prevention and treatment*. London: Royal College of Physicians, 1996:1-10.
- 18 Torgerson DJ, Bell-Syer SE. Hormone replacement therapy and prevention of non-vertebral fractures: a meta-analysis of randomised trials. *JAMA* 2001;285:2891-7.
- 19 Grodstein F, Stampfer M. The epidemiology of coronary heart disease and estrogen replacement in postmenopausal women. *Prog Cardiovasc Dis* 1995;38:199-210.
- 20 Grady D, Gebretsadick T, Kerlikowske K, Ernster V, Petitti D. Hormone replacement therapy and endometrial cancer risk: a meta-analysis. *Obstet Gynaecol* 1995;85:304-13.
- 21 Hulley S, Furberg C, Barrett-Connor C, Cauley J, Grady D, Haskell W, et al. Non-cardiovascular disease outcomes during 6.8 years on hormone therapy: heart and estrogen/progestin replacement study follow up (HERS II). *JAMA* 2002;288:58-66.
- 22 Grady D, Herrington D, Bittner V, Davidson M, Hlatky M, Hsia J, et al. Cardiovascular disease outcomes during 6.8 years of hormone therapy: heart and estrogen/progestin replacement study follow-up (HERS II). *JAMA* 2002;288:49-57.
- 23 Daly E, Vessey MP, Hawkins MM, Carson JL, Gough P, Marsh S. Risk of venous thromboembolism in users of HRT. *Lancet* 1996;348:977-80.
- 24 Jick H, Derby LE, Myers MW, Vasilakis C, Newton KM. Risk of hospital admission for idiopathic venous thromboembolism among users of postmenopausal oestrogens. *Lancet* 1996;348:981-3.
- 25 Grady D, Wenger NK, Herrington D, Khan S, Furberg C, Hunnigake D, et al. Postmenopausal hormone replacement therapy increases risk for venous thromboembolism disease: the heart and estrogen/progestin replacement study. *Ann Intern Med* 2000;132:689-96.
- 26 Grodstein F, Newcomb PA, Stampfer MJ. Postmenopausal hormone therapy and the risk of colorectal cancer: a review and meta-analysis. *Am J Med* 1999;106:574-82.
- 27 Hunter MS, O'Dea I. Perception of future health risks in mid-aged women: estimates with and without behavioural changes and hormone replacement therapy. *Maturitas* 1999;33:37-43.
- 28 Collaborative Group on Hormonal Factors in Breast Cancer. Breast cancer and hormone replacement therapy: collaborative reanalysis of data from 51 epidemiological studies of 52,705 women with breast cancer and 108,411 women without breast cancer. *Lancet* 1997;350:1047-59.
- 29 Beresford S, Weiss NS, Voigt LF, McKnight B. Risk of endometrial cancer in relation to use of oestrogen combined with cyclic progestogen therapy in postmenopausal women. *Lancet* 1997;349:458-61.
- 30 Weiderpass E, Adami HO, Baron JA, Magnusson C, Bergstrom R, Lindgren A, et al. Risk of endometrial cancer following estrogen replacement with and without progestins. *J Natl Cancer Inst* 1999;91:1131-7.
- 31 Sturdee DW, Ulrich LG, Barlow DH, Wells M, Campbell MJ, Vessey MP, et al. The endometrial response to sequential and continuous combined estrogen/progestogen replacement therapy. *Br J Obstet Gynaecol* 2000;107:1392-400.
- 32 Wells M, Sturdee D, Barlow DH, Ulrich LG, O'Brien K, Campbell MJ, et al. Effect on endometrium of long term treatment with continuous combined oestrogen-progestogen replacement therapy: follow up study. *BMJ* 2002;325:239.
- 33 Lacey JV, Mink PJ, Lubin JH, Sherman ME, Troisi R, Hartge P, et al. Menopausal hormone replacement therapy and risk of ovarian cancer. *JAMA* 2002;288:334-41.
- 34 Raudaskoski T, Tapanainen J, Tomas E, Luoto H, Pekonen F, Ronni-Sivula H, et al. Intrauterine 10 microgm and 20 microgm levonorgestrel systems in postmenopausal women receiving oral oestrogen therapy: clinical, endometrial and metabolic response. *Br J Obstet Gynaecol* 2002;109:136-44.

Lesson of the week

Misdiagnosis of epilepsy in patients prescribed anticonvulsant drugs for other reasons

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Doctors must be clear to patients and other doctors when prescribing anticonvulsants for conditions other than epilepsy

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Up to a fifth of patients referred to neurology clinics with refractory epilepsy have psychogenic non-epileptic seizures.¹ Sexual abuse has been suggested as a cause in some patients,² but in many the aetiology remains unclear.

Anticonvulsant drugs are now commonly used for indications such as pain or stabilising mood.³ We describe two patients who were prescribed anticonvulsants for reasons other than epilepsy and who went on to develop blackouts that were misdiagnosed as epilepsy. Misinterpretation of anticonvulsant treatment as evidence for epilepsy was a crucial factor.

Case reports

The patients were assessed at the Glasgow non-epileptic seizures clinic between January 2000 and May 2001. Video electroencephalography confirmed the diagnosis of non-epileptic seizures. Prolonged interictal electroencephalographic recording and detailed analysis of eyewitness accounts of attacks showed no evidence of concomitant epilepsy.

Case 1

A 62 year old man with no predisposing factors for epilepsy had a history of insulin dependent diabetes. He was prescribed carbamazepine in January 1998 to

control his severe neuropathic pain. In June 1999, he developed brief attacks, which consisted of tremor with occasional loss of responsiveness. Investigations included brain computed tomography and electroencephalography. His computed tomographic appearances were normal. Two attacks occurred during electroencephalography, and no epileptiform abnormality was seen. Despite this, the patient was referred to a neurologist with "possible epilepsy." He was prescribed sodium valproate because of lack of efficacy of his previous anticonvulsant, carbamazepine.

The attacks did not respond to anticonvulsants, and he was referred to a non-epileptic seizures clinic in August 2000 because of doubts about the cause of his seizures. A diagnosis of non-epileptic seizures was confirmed and anticonvulsant treatment was withdrawn. The patient was referred to a psychologist and became attack free. He remained so in May 2002.

Case 2

A 29 year old right handed man presented in 1995 with pain, spasm, and tremor of the lower right leg. He had division of the terminal filament for a tethered spinal cord, which was thought to be the cause of his symptoms. He improved, but in 1996 he was readmitted to hospital with paraesthesia and leg spasms and was prescribed carbamazepine by a neurologist.

Carbamazepine was continued until 1997, when he had several emergency admissions to a different hospital for painful leg spasms. During these admissions he had episodes of apparent loss of consciousness with “shaking” of the right leg. Electroencephalography showed non-epileptiform abnormalities. However, the report raised the possibility that the changes were due to epilepsy. A discharge document from one of these admissions stated that the patient had had generalised seizures for six months and right sided focal seizures for many years.

By early 1998, his symptoms of leg spasm and pain had subsided, but he was reporting episodes of generalised jerking and loss of consciousness. Electroencephalography at this time was reported as showing abnormalities that sometimes had “an epileptiform configuration.” After an episode later in 1998, he attended the accident and emergency department of another hospital and was treated with intravenous diazepam for what were referred to in the case record as “prolonged epileptic seizures.” It was noted in the discharge letter that “he has had focal seizures for many years and continuation of his usual carbamazepine is recommended.”

In 1999, he was re-referred to a neurologist after admission to a general hospital, and the referral letter mentioned the possibility of pseudoseizures. The interictal electroencephalogram was again reported as showing non-specific abnormalities. He continued taking carbamazepine, which was by now referred to in the notes as anticonvulsant treatment. At review, the neurologist expressed doubt about the diagnosis, and in 2000, the patient was referred to an epilepsy specialist with the possible diagnosis of non-epileptic seizures. The diagnosis was confirmed by video electroencephalography. His past electroencephalograms were reviewed, and it was felt that in fact there had been no clear epileptiform activity.

Carbamazepine was withdrawn, and the patient was referred to a psychologist. Apart from a short relapse, he has remained attack free.

Discussion

Patients with non-epileptic seizures are often prescribed anticonvulsant drugs because of misdiagnosis of epilepsy, and many have been taking these drugs for some time.⁴ The drugs are not normally prescribed until after development of the attack disorder. Therefore, although anticonvulsants might have a role in maintaining or reinforcing non-epileptic seizures in these patients, they are not usually a credible cause.

In our patients, however, prescription of anticonvulsant drugs preceded the development of the attack disorder by at least a year. It was clear from the case notes that the anticonvulsants had an important role in determining doctors’ beliefs about the diagnosis. This may have been particularly important when patients presented to accident and emergency departments, where case records are not readily available and medical history may be inferred from drug history.

High levels of suggestibility have often been reported in patients with non-epileptic seizures.⁵ A developing medical assumption that anticonvulsant treatment was being used for epilepsy may also have influenced our patients’ beliefs. A doctor reading in the

notes that the patient was taking anticonvulsants might direct initial questioning to episodes of loss of consciousness, possibly even mentioning epilepsy, thus suggesting the symptom and the disease to the patient. This may contribute to the genesis of non-epileptic seizures.

Although the prescription of anticonvulsants seemed to be the main factor in the assumption that these patients had epilepsy, electroencephalography also contributed. In the first case, no changes were seen during attacks recorded by electroencephalography. This finding would normally be regarded as highly suggestive of non-epileptic seizures, but in this case it was ignored. In the second case, over-reporting of non-specific abnormalities clearly reinforced the diagnosis of epilepsy once the attack disorder was established. One study has identified overinterpretation of such abnormalities as a common reason for overdiagnosis of epilepsy.⁶

In both our patients non-epileptic seizures took over from the original complaint and became the main health problem. Such seizures are associated with social and economic disadvantages as well as iatrogenic risks associated with the emergency treatment of pseudostatus epilepticus⁷ and long term anticonvulsant treatment. The effect on patients’ lives and the lives of those around them is profound.

A mistaken assumption that anticonvulsant drugs are prescribed for epilepsy may contribute to establishing an erroneous diagnosis and may play a part in the genesis of non-epileptic seizures by influencing patients’ beliefs. It is important that the prescribing physician is clear to patients and other doctors that the anticonvulsant drug is not prescribed for epilepsy.

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- 1 Betts T. Pseudoseizures: seizures that are not epilepsy *Lancet* 1990;336:163-4.
- 2 Francis P, Baker G. Non-epileptic attack disorder (NEAD): a comprehensive review. *Seizure* 1999;8:53-61.
- 3 Malt UF. The basis for the use of antiepileptic drugs in psychiatric disorders. *Acta Neurol Scand* 2000;102 (suppl):40-2.
- 4 Leis AA, Ross MA, Summers AK. Psychogenic seizures: ictal characteristics and diagnostic pitfalls. *Neurology* 1994;42:95-9.
- 5 Barry JJ, Atzman O, Morell MJ. Discriminating between epileptic and nonepileptic events: the utility of hypnotic seizure induction. *Epilepsia* 2000;41:81-4.
- 6 Smith D, Defalla BA, Chadwick DW. The misdiagnosis of epilepsy and management of refractory epilepsy in a specialist clinic. *Q J Med* 1999;92:15-23.
- 7 Howell SJL, Owen L, Chadwick DW. Pseudostatus epilepticus. *Q J Med* 1989;71:507-19.

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Endpiece

Paper thin

The division between art and deviousness and crime is sometimes as thin as a cigarette paper.

Robertson Davies (1913-95), *What's bred in the bone*, London: Penguin, 1986

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