18 Burton JL, Halim MM, Meyrick G, Jeans WD, Murphy D. Male pattern alopecia and masculinity. *Br J Dermatol* 1979;100:567-71.
19 Norstrom RE. Synchronous balding of scalp and hair bearing grafts of scalp transplanted to the skin of the arm in male pattern baldness. *Acta Derm Venereol* 1979;59:266-8.
20 Orentreich N. Autografts in alopecias and other selected dermatological conditions. *Ann NY Acad Sci* 1959;83:462.
21 Randall VA, Thornton MJ, Messenger AG. Cultured dermal papilla cells from androgen-dependent human hair follicles (eg beard) contain more androgen receptors than those from non-balding areas of the scalp. *J Endocrinol* 1992;133:141-7.
22 Itami S, Kurata S, Takayasu S. 5α reductase activity in cultured dermal papilla cells from beard compared with reticular dermal fibroblasts. *J Invest Dermatol* 1990;94:150-2.
23 Kuster W, Happle R. The inheritance of common baldness: two B or not two B? *J Am Acad Dermatol* 1984;11:921-6.
24 Ellis JA, Stebbing M, Harrap SB. Genetic analysis of male pattern baldness and 5α reductase genes. *J Invest Dermatol* 1998;110:849-53.
25 Cash TF. The psychological effects of androgenetic alopecia in men. *J Am Acad Dermatol* 1992;26:926-31.
26 Cash TF, Butters JW. Poor body image: helping the patient to change. *Med Aspects Hum Sexuality* 1988; 22:67-70.
27 Orentreich D, and Orentreich N. Androgenetic alopecia and its treatment, a historical view. In: Unger WP, ed. *Hair transplantation*. 3rd ed. New York: Marcel Dekker, 1995:1-33.
28 Hecht A. Hair grower and hair-loss prevention drugs. *FDA Consumer*, 1985 April 19:1-3.
29 Savin RC. Use of topical minoxidil in the treatment of male pattern baldness. *J Am Acad Dermatol* 1987;16:696-704.
30 Olsen EA, Weiner MS. Topical minoxidil in male pattern baldness: effects of discontinuation of treatment. *J Am Acad Dermatol* 1987;17:97-101.
31 Olsen E. Finasteride (1 mg) in the treatment of androgenetic alopecia in men [abstract]. *Aust J Dermatol* 1997;38;A316.
32 Rushton DH, Norris MJ, Ramsay ID. Topical 0.05% finasteride significantly reduced serum DHT concentrations, but had no effect in preventing the expression of genetic hair loss in men. In:Van Neste D, Randall VA, eds. *Hair research for the next millennium*. Amsterdam: Elsevier, 1996:359-62.
33 Unger WP. Surgical approach to hair loss. In: Olsen EA, ed. *Disorders of hair growth. Diagnosis and treatment*. New York: McGraw-Hill, 1994:353-74.
34 Lepaw MI. Complications of implantation of synthetic fibres into scalps for 'hair' replacement: experience with fourteen cases. *J Dermatol Surg Oncol* 1979;5:201-4.
35 Chen W, Zouboulis CC, Orfanos CA. The 5α reductase system and its inhibitors. Recent development and its perspective in treating androgen dependent skin disorders. *Dermatol* 1996;193:177-84.
36 Li L, Hoffman RM. The feasibility of targeted selective gene therapy of the hair follicle. *Nature Med* 1995;1:705-6.

(Accepted 12 February 1998)

Lesson of the week

Treatment resistant epilepsy or convulsive syncope?

Amir Zaidi, Peter Clough, Bruce Scheepers, Adam Fitzpatrick

A primary cardiac problem should always be considered in patients with apparent epilepsy who respond poorly to treatment

Manchester Heart Centre, Royal Infirmary, Manchester M13 9WL
Amir Zaidi, *research fellow*
Adam Fitzpatrick, *consultant cardiologist*
David Lewis Centre for Epilepsy, Warford, Alderley Edge, Cheshire SK9 7UD
Peter Clough, *clinical medical officer*
Bruce Scheepers, *consultant neuropsychiatrist*
Correspondence to: Dr Zaidi amir@mhc.cmht.nwest.nhs.uk

BMJ 1998;317:869–70

The diagnosis of epilepsy is complicated by various conditions that can mimic an epileptic seizure, and cardiovascular conditions causing syncope may account for many cases of so called secondary seizures.[1] Convulsive syncope—that is, cerebral anoxic seizure activity secondary to transient global impairment of blood flow—can be difficult to differentiate from epilepsy. The differentiation is, however, important because syncope can be treated effectively, especially when it is due to a bradycardia.[1] In addition, long term anticonvulsant treatment is expensive and can cause serious morbidity.[2] We present the cases of three patients thought to have treatment resistant epilepsy who were subsequently found to have a cardiac condition.

Case histories

Case 1

A 32 year old woman was referred to the epilepsy clinic in January 1995 with a four year history of recurrent blackouts. She described episodes in which she became weak and had to lie on the floor followed by loss of consciousness lasting for about 1 minute with clenching of her fist and sometimes jerking, especially of the legs, but no incontinence or tongue biting. She normally recovered quickly, although she was tired afterwards. The episodes occurred up to four times a week. In 1991, a 72 hour electroencephalogram had given normal results, but a trace taken after sleep deprivation showed some left sided slow wave changes. She was started on phenytoin for presumed epilepsy. She subsequently tried several anticonvulsant drugs including lamotrigine, sodium valproate, clobazam, vigabatrin, carbamazepine, and gabapentin with no significant improvement apart from a short period when clobazam was introduced. Her condition had deteriorated with gabapentin.

At referral she was taking clobazam, vigabatrin, and carbamazepine. She was changed to carbamazepine only (800 mg daily) with little effect on the frequency of attacks. Repeat ambulatory electroencephalography and magnetic resonance imaging of the brain gave normal results. She was admitted to the David Lewis Centre in November 1996 for assessment. She had a typical attack during ambulatory electroencephalographic monitoring. Immediately before the attack a sinus pause of about 5 seconds was recorded on her electrocardiogram, and she was transferred to a coronary care unit for further assessment. Electrocardiographic monitoring showed frequent sinus pauses lasting up to 7 seconds. A dual chamber permanent pacemaker was implanted and her blackouts resolved completely.

Case 2

A 43 year old man was referred for a neurological opinion in 1991 with a six year history of recurrent funny turns. He developed buzzing in his right ear followed by severe dizziness but no loss of consciousness. Thorough investigations at his local hospital had produced no clear diagnosis. Electroencephalography and computed tomography of the brain showed no abnormality. In February 1992 he had an attack complicated by loss of consciousness and a convulsion. Epilepsy was diagnosed, and he was started on carbamazepine. However, he continued to have blackouts about every three months despite plasma anticonvulsant concentrations within the therapeutic range. He was referred to the Manchester Heart Centre in September 1992. Electrocardiography, echocardiography, and 24 hour Holter monitoring and carotid sinus massage gave normal results but he remained under yearly review. He had a tilt test[3] in October 1995 after a cluster of blackouts. After 32 minutes of 60° head up tilt he developed a sudden nodal bradycardia of 20 beats/minute with syncope in keeping with a diagnosis of vasovagal syncope.[4] He had a dual chamber pacemaker inserted in April 1996 and anticonvul-

sant treatment was stopped in December 1996. He has been asymptomatic since insertion of the pacemaker.

Case 3

A 72 year old woman was referred to the Manchester Heart Centre in January 1997 with eight seizure-like episodes over 13 years. She would become pale and cool before blacking out, when she became rigid, her eyes open and staring, and unresponsive to speech. She recovered within 2-3 minutes, but vomited on regaining consciousness. Epilepsy had been diagnosed in 1990 when her electroencephalogram had shown a temporal lobe abnormality, and she had been started on carbamazepine. However, she had had five further episodes despite carbamazepine in doses up to 1200 mg daily. Cardiac investigation had previously shown no abnormality. She had a 60° head up tilt test in February 1997. After 30 minutes her blood pressure dropped suddenly to 83/50 mm Hg with presyncope and severe distress and the test was stopped. The carbamazepine was discontinued, and she was started on atenolol for vasodepressor vasovagal syncope. She has had no further convulsive episodes over the past 12 months.

Comment

The causes of sudden loss of consciousness are extensive, but they are broadly neurological and cardiovascular. The most important differentiation is that of convulsive syncope from epilepsy, the main neurological deficit. Our three patients all improved greatly with specific treatment, but only after many years of being labelled as epileptic. As well as the attendant social and psychological difficulties they had ineffective drug treatment, made repeated hospital visits, and had enormously costly and unhelpful investigation. Each was eventually diagnosed by simple and inexpensive tests (electrocardiography or head up tilt testing).

Accurate and early diagnosis of convulsive syncope is important. Cardiac rhythm can be affected by anticonvulsant drugs, particularly carbamazepine, which is associated with atrioventricular block.[5 6] In addition, severe episodic bradycardia and ventricular tachyarrhythmias are potentially life threatening and require urgent cardiological intervention. The reported one year mortality of patients with a cardiac cause of syncope is 18-33%[1 7–10] compared with 3-6% for syncope of unknown origin.[7–9] Reflex forms of syncope (vasovagal syncope and carotid sinus syncope) seem to carry little risk of death but are associated with a high incidence of injury, particularly in elderly people.[1–11]

Reflex syncope may account for many cases of convulsive syncope. Lin et al reported convulsive episodes in up to 12% of blood donors with vagally mediated syncope.[12] Grubb et al found that six of 15 patients with recurrent unexplained seizure-like episodes unresponsive to anticonvulsant drugs had tonic-clonic seizures during baseline head up tilt testing.[13] A further four patients had seizure-like activity with isoprenaline infusion during head up tilting. After treatment (permanent pacing in two patients, drugs in the others) all 10 patients were free from seizures and had negative tilt test results. Five of these patients had electroencephalography, all of whom had diffuse brain wave slowing. Some workers have suggested that convulsive syncope can be reliably distinguished from epilepsy by the brief duration of the ictal phase, lack of rhythmic clonic movements, rapidity of recovery, and absence of post-ictal phenomena[14–16] but these are insufficiently reliable or specific to be standardised against more stringent diagnostic criteria.[2] Furthermore, abnormal movements accompanying loss of consciousness may vary within patients.

Patients with presumed epilepsy who respond poorly to treatment should have their attacks re-examined, particularly when their electroencephalogram appears normal or non-specifically abnormal. If there is doubt about epilepsy, monitoring of attacks and referral for a cardiological opinion should be considered. All such patients should have a resting 12 lead electrocardiogram, which may be diagnostic—for example, in Wolff-Parkinson-White syndrome or congenital long QT syndrome. If the electrocardiogram appears normal the cause is unlikely to be ventricular tachyarrhythmia.[7] The case for routine Holter monitoring to identify transient arrhythmias is more difficult. The diagnostic yield of continuous 72 hour Holter monitoring is only 2-4% in syncope,[17 18] but an electrocardiographic channel should be included routinely during ambulatory electroencephalography. Convulsive vasovagal syncope should be considered in patients with treatment resistant epilepsy. Although head up tilt testing has limited sensitivity and specificity (both 80-90%), it is safe, inexpensive, and increasingly widely available.

Misdiagnosis of epilepsy remains a major clinical problem. One way forward is for cardiologists, neurologists, and psychiatrists to collaborate in the investigation of fits, faints, and blackouts. This should improve the speed and accuracy of diagnosis and eliminate unnecessary and costly investigation or prolonged, unnecessary, and potentially dangerous treatments.

1 Kapoor WN. Evaluation and management of the patient with syncope. *JAMA* 1992;268:2553-60.
2 Shorvon S. When should anticonvulsant treatment be started? In: Ross E, Chadwick DW, Crawford RJ, eds. *Epilepsy in young people*. Chichester: Wiley, 1987:3-46.
3 Fitzpatrick AP, Sutton R. Tilting towards a diagnosis in unexplained recurrent syncope. *Lancet* 1989;i:658-60.
4 Sutton R, Petersen MEV. The clinical spectrum of neurocardiogenic syncope. *J Cardiovasc Electrophysiol* 1995;6:569-76.
5 Boessen F, Anderson EB, Jensen EK, Ladefoged SD. Cardiac conduction disturbances during carbamazepine therapy. *Acta Neurol Scand* 1983;68:49-52.
6 Beerman B, Edhag O, Vallin H. Advanced heart block aggravated by carbamazepine. *Br Heart J* 1977;i:754-5.
7 Kapoor WN. Evaluation and outcome of patients with syncope. *Medicine (Balt)* 1990;69:160-75.
8 Silverstein MD, Singer DE, Mulley A, Thibault GE, Barnett GO. Patients with syncope admitted to medical intensive care units. *JAMA* 1982;248:1185-9.
9 Kapoor W, Karpf M, Wieand S, Peterson J, Levey G. A prospective evaluation and follow-up of patients with syncope. *N Engl J Med* 1983;309:197-204.
10 Day SC, Cook EF, Funkenstein H, Goldman L. Evaluation and outcome of emergency room patients with transient loss of consciousness. *Am J Med* 1982;73:15-23.
11 Manolis AS, Linzer M, Salem D, Estes NAM. Syncope: current diagnostic evaluation and management. *Ann Intern Med* 1990;112:850-63.
12 Lin JT, Ziegler DK, Lai CW, Bayer W. Convulsive syncope in blood donors. *Ann Neurol* 1982;11:525-8.
13 Grubb BP, Gerard G, Roush K, Temesy-Armos P, Elliott L, Hahn H, et al. Differentiation of convulsive syncope and epilepsy with head-up tilt testing. *Ann Intern Med* 1991;115:871-6.
14 Gastaut H, Fisher-William M. Electroencephalographic study of syncope: its differentiation from epilepsy. *Lancet* 1957;ii:1018-25.
15 Duvoisin RC. Convulsive syncope induced by the Weber manoeuvre. *Arch Neurol* 1962;7:219-26.
16 Klein LJ, Saltzman HA, Heyman A, Sieker HO. Syncope induced by the Valsalva maneuvre: a study of the effects of arterial blood gas tensions, glucose concentrations and blood pressure. *Am J Med* 1964;37:263-8.
17 DiMarco JP, Philbrick JT. Use of electrocardiographic (Holter) monitoring. *Ann Intern Med* 1990;113:53-68.
18 Gibson TC, Heitzman MR. Diagnostic efficacy of 24-hour electrocardiographic monitoring for syncope. *Am J Cardiol* 1984;53:1013-7.

(Accepted 4 February 1998)