Saturday 2 March 2002

BMJ

The misdiagnosis of epilepsy

The rate of misdiagnosis and wide treatment choices are arguments for specialist care of epilepsy

The case of Dr Andrew Holton, consultant paediatrician at Leicester Royal Infirmary, highlights once again some of the dangers and pitfalls in the diagnosis and management of epilepsy. He has been suspended and referred to the General Medical Council after a review of 214 children seen by him showed that 171 gave definite or possible "cause for concern." Just over a third of the children were not thought to have had epilepsy, and just under a third were thought to have been overtreated.[1] Both are common pitfalls in the management of epilepsy.

The review also made clear that Dr Holton's training fell well short of what would be required for his post. Although a consultant in paediatrics, Dr Holton was not a paediatric neurologist, of whom there are just 62 in the United Kingdom. The report also points to professional isolation and under-resourcing as important mitigating factors in Dr Holton's practice. This episode graphically illustrates the potential consequences of the shortcomings identified in 2000 by the Clinical Standards Advisory Group in its report on epilepsy services in the United Kingdom.[2]

Though the diagnosis of seizures and epilepsy can be straightforward, it can also be one of the greatest clinical challenges. An adequate diagnosis requires differentiation between seizures and other causes of transient neurological disturbance and collapse; differentiation between acute symptomatic and unprovoked truly epileptic seizures; and, in people with epilepsy, classification of the disorder and identification of the cause so as to optimise treatment.

The symptoms of epileptic seizures are varied and there are many imitators, ranging from convulsive syncope through to psychogenic events. The phenomenon most commonly mistaken for a convulsive seizure is syncope. Classical teaching is that collapse in syncope is flaccid and that no motor activity occurs.[3] Commonly occurring motor and ocular phenomena are not widely recognised. Lempert et al induced syncope in 42 healthy volunteers, 90% of whom experienced myoclonus, usually multifocal.[4] Additional features such as head turning, oral movements, or attempts to sit up occurred in 80%. These motor phenomena are often taken to indicate that a seizure has occurred. Similar convulsive episodes seen immediately after concussive head injury may also be mistaken for epileptic phenomena.[5]

Neurogenic syncope is provoked and involves brief loss of consciousness and rapid recovery. A detailed history will usually be all that is required by an experienced clinician to differentiate this from seizures. Unfortunately, in inexpert hands inappropriate investigation often takes precedence. Fainting is probably the single commonest reason for requesting an electroencephalogram, which in 20% of the population will reveal non specific abnormalities open to misinterpretation.[6] Given that most requests emanate from non-specialist settings and most electroencephalograms are reported by neurophysiologists without great experience of epilepsy and its management, there is considerable potential for misdiagnosing faints as seizures.

Cardiac syncope often causes immediate loss of consciousness, tonic stiffening of body and limbs, and often myoclonic jerking. Testing with a tilt table and electrocardiographic monitoring may be needed to identify a specific cause and avoid the erroneous diagnosis of epilepsy.[7 8]

A population based study in Rochester, Minnesota, indicates that 40% of incident seizures are symptomatic of an acute systemic or cerebral disturbance rather than epilepsy.[9] Fever in children and alcohol withdrawal in adults are the commonest causes of such acute symptomatic seizures. Recognition prevents unnecessary antiepileptic drug treatment and avoidance of the provocative factor, or treatment of the underlying cause, and permits early resumption of driving.

Dr Holton's experience is probably no more than the tip of the iceberg. Smith et al reported on 184 consecutive patients referred to one consultant neurologist.[10] Forty six were believed to have been misdiagnosed, of whom 12 were referred with drug resistant epilepsy. Nineteen had experienced side effects of drugs, 12 had unnecessary driving restrictions, and five had serious employment problems with three dependent on state benefits. Zaidi et al, using standard laboratory tests, found that 13 of 36 (31%) patients with continued attacks despite antiepileptic drugs had treatable cardiovascular conditions.[8] The direct costs to the NHS due to fruitless outpatient visits and unnecessary investigations and drugs are difficult to quantify. However, if one applies the figures from the cost of illness study by Cockerell et al to only those misdiagnosed patients with apparently drug resistant epilepsy the total cost of misdiagnosis is estimated to be £125m a year.[11]

BMJ 2002;324:495–6

While the rate of misdiagnosis by itself is a strong argument for specialist care of epilepsy, the advances and increased choice of pharmacological and other treatments further support the case. We can no longer accept the delivery of epilepsy care from an unsupported general physician or paediatrician. The report of the Clinical Standards Advisory Group on epilepsy services recommends structured multidisciplinary specialist care for people with epilepsy with an appropriate interface with primary care.[2] The poor quality of epilepsy services and the preventable mortality of epilepsy have recently been highlighted in the chief medical officer's annual report and commitments made to address these issues.[12] It must now be evident that the human and financial costs of failing to implement the recommendations are too high to be acceptable.

David Chadwick *professor of neurology*
David Smith *consultant neurologist*

Walton Centre for Neurology and Neuroscience, Liverpool L9 7LJ

1 White C. Doctor referred to GMC after inquiry into epilepsy diagnoses. *BMJ* 2001;323:1323.
2 Kitson A, Shorvon S, Clinical Standards Advisory Group. *Services for patients with epilepsy*. London: Department of Health, 2000.
3 Petch MC. Syncope. *BMJ* 1994;308:1251-2.
4 Lempert T, Bauer M, Schmidt D. Syncope: a videometric analysis of 56 episodes of transient cerebral hypoxia. *Annals of Neurology* 1994;36:233-7.
5 McCrory PR, Bladin PF, Berkovic SF. Retrospective study of concussive convulsions in elite Australian rules and rugby league footballers: phenomenology, aetiology, and outcome. *BMJ* 1997;314:171-4.
6 Smith D, Bartolo R, Pickles RM, Tedman BM. Requests for electroencephalography in a district general hospital: retrospective and prospective audit. *BMJ* 2001;322:954-7.
7 Zaidi A, Cotter L, Fitzpatrick A. Head up tilt testing has a place in distinguishing certain conditions from epilepsy. *BMJ* 1997;314:1048.
8 Zaidi A, Clough P, Cooper P, Scheepers B, Fitzpatrick AP. Misdiagnosis of epilepsy: many seizure-like attacks have a cardiovascular cause. *J Am Coll Cardiol* 2000;36:181-4.
9 Annegers JF, Hauser WA, Lee JR, Rocca WA. Incidence of acute symptomatic seizures in Rochester, Minnesota, 1935-1984. *Epilepsia* 1995;36:327-33.
10 Smith D, Defalla BA, Chadwick DW. The misdiagnosis of epilepsy and the management of refractory epilepsy in a specialist clinic. *QJM* 1999;92:15-23.
11 Cockerell OC, Hart YM, Sander JWAS, Shorvon SD. The cost of epilepsy in the United Kingdom: An estimation based on the results of two poulation-based studies. *Epilepsy Research* 1994;18:249-60.
12 CMOs report. http://www.doh.gov.uk/cmo/annualreport2001/introduction.htm (Accessed 14 January 2002).

Surgery for temporal lobe epilepsy

Highly effective but remains underused

In a worldwide review of epilepsy surgery carried out in 1985, 53 centres were found that had undertaken about 3500 operations for intractable epilepsy. Five years later this had increased to over 8000 operations done in 118 centres.[1] In both surveys most patients underwent resections for temporal lobe epilepsy. Specialist services for epilepsy and intensive electroencephalography monitoring are now more widely available and presurgical evaluation has become easier due to advances in neuroimaging.

Any doubts that surgery is not effective have been dispelled by a recent randomised study.[2] Patients were assigned to surgery or a one year waiting list control group where they received optimum medical treatment. This study design avoided any ethical objections to delaying surgery. Fortunately, only 10% of the patients were excluded after investigation so an appropriate intention to treat analysis could be undertaken. With medical treatment only 5% remitted, while after surgery 65% were completely seizure free. The study design did however restrict comparative outcomes to one year of follow up, which is rather short. Despite this, surgery was associated with sustained and major improvements in quality of life. While drug treatment remains very helpful in suppressing seizures or making them less severe, surgery offers a high probability of complete remission. With modern investigative and operative techniques, it is curious that large numbers of people with chronic temporal lobe epilepsy are still not referred for what in many can be a curative treatment. Hopefully, further randomised studies will now be done with more relevant treatment options comparing the type or timing of operation.

The commonest pathology in chronic temporal lobe epilepsy is mesial temporal sclerosis with scarring of the hippocampus.[3] The other major cause is a curious form of indolent tumour containing both neuronal and glial elements, often occurring in the mesial temporal area. Having defied classification for many years it is now thought to be a benign embryological tumour.[4] Less commonly visible on conventional *x* ray computerised tomography, both lesions can now be clearly seen on high resolution magnetic resonance imaging.[5] In the early 1950s Falconer at the Maudsley Hospital developed the en bloc temporal lobectomy, which removed the anterior temporal neocortex, the amygdala, and the body of the hippocampus. Postoperative deficits, particularly dysphasia and hemianopia, were minimised by keeping to set anatomical landmarks. Eighty per cent of patients became seizure free when the specimen showed mesial temporal sclerosis or an indolent tumour and the worst outcome occurred when normal brain was removed. With modern imaging this is less likely but otherwise the results of surgery now are remarkably similar to those quoted by Falconer. A randomised study has shown that additional removal of the posterior tail of the hippocampus improves outcome.[6]

It is difficult to find exact epidemiological data on the total numbers of people suitable for temporal lobe surgery. Most have complex partial seizures, typically an epigastric, affective, or psychic aura, followed by staring, chewing movements, and automatisms in the limbs. The seizures must be disabling, usually occurring every week and resistant to both first and second line drugs taken to maximum tolerated doses. Janz has estimated that about 17 new patients per million of the population per year are likely to fulfil these criteria.[7] Despite the expansion of epilepsy surgery it is likely that only a fraction of this number are referred and there is in addition a large group of unoperated cases that have accumulated over many years.[8]

Centres undertaking epilepsy surgery should aim to expand their practice quickly and should probably do at least two operations per month.[9] Operative skills need to be maintained so that the risk of stroke is kept

BMJ 2002;324:496–7