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vCJD

Variant Creutzfeldt-Jakob disease

R G Will

How new is new?

If variant Creutzfeldt-Jakob disease (vCJD) is caused by bovine spongiform encephalopathy (BSE) it must be a new disease, as human exposure to the BSE agent is unlikely to have happened much before 1983.¹ The study by Hillier *et al* (this issue, pp 304–309)² adds significantly to the evidence supporting the hypothesis that vCJD really is a new disease, with the caveat that the study unavoidably had incomplete follow up data. No previously unrecognised cases of vCJD were found in a systematic retrospective study in Wales, which included review and restaining of available neuropathological tissue. A similar study based on death certificates in England and Wales between 1979 and 1996 also failed to identify missed cases of vCJD³ and no case with a similar neuropathological phenotype to vCJD has been identified in any country despite extensive review of archival neuropathology tissues. Although there are still doubters,⁴ informed opinion supports the view that vCJD really is a new disease.^{5,6} It is important to recognise that the availability of stored brain samples was critical to the identification of vCJD⁷ and to the study of Hillier *et al*. Defending medical activities deemed by some to be ethically controversial is essential both for research and informed clinical practice.⁸

Although the clinical features of the first three cases of vCJD were judged to be “well within the recognised diagnostic spectrum for CJD”,⁹ the neurological

phenotype of vCJD is relatively distinct from sporadic CJD and also fairly consistent between cases.¹⁰ The implication is that it is likely that cases of vCJD are being identified in life by neurologists and, assuming notification to the surveillance system, that the figures on numbers of cases of vCJD are accurate. There is a separate surveillance system for vCJD in children,¹¹ which has led to the identification of six cases of vCJD where the patient's age was less than 16 years at onset of symptoms. The diagnosis of vCJD has been confirmed in a patient aged 74 years,¹² significantly extending the age range and raising questions about the efficiency of surveillance in elderly people. Accuracy of data on the numbers of cases of vCJD is critical to public health planning and to both short term and long range forecasts of the future of the vCJD epidemic.

Analyses of short term trends in vCJD have been published¹³ and currently indicate an approximate doubling in the number of cases of vCJD in the United Kingdom every 3 years. Longer term predictions of vCJD numbers have been more controversial with a wide range of future scenarios varying between a total of just over 200 cases,¹⁴ a few thousand cases¹⁵ and over 130 000 cases.¹⁶ This variation reflects the many uncertainties about BSE and vCJD, including the extent of human exposure to BSE, the level of the species barrier between bovine and human, and variations in host susceptibility—to date all tested

cases of vCJD have been homozygous for methionine at codon 129 of the prion protein gene. One important variable in all estimates of vCJD numbers is the year cases first appeared. The paper by Hillier *et al*² provides important support to the hypothesis that vCJD is a new disease which really did first appear in the mid-1990s.

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Dystonia

Dystonia in multiple system atrophy

D E Riley

Dystonia is often encountered in untreated MSA

In this issue (pp 300–303) Boesch *et al* report on their experience with dystonia in multiple system atrophy (MSA).¹ They correctly point out the relative neglect of dystonia in previous clinical descriptions of patients with MSA. In 1986, Adams declared that dystonia was “not part of the clinical tableau” of striatonigral degeneration,² a quarter of a century after he described the disease. (Striatonigral degeneration corresponds to the MSA-P designation, carried by the bulk of the patients of Boesch *et al*, of current diagnostic classifications of MSA). Even when discussion focused on the motor problems caused by MSA, dystonia was not mentioned.³ These influential writings have led us to discount the likelihood of MSA causing a combination of dystonia and parkinsonism in favour of other diagnoses, such as Parkinson's disease or corticobasal degeneration.

Much as in Parkinson's disease, dystonia may be a direct manifestation of MSA or the result of treatment with dopaminergic agents. The highest previously recorded prevalence of dystonia in MSA was 12%.⁴ In the current report, dystonia was documented in 46% of

untreated patients with MSA. Antecollis accounted for most of the dystonia encountered in these patients, with focal limb dystonias comprising the rest. Of note, disease related focal limb dystonia improved on levodopa in five of five patients. Over 80% of patients with a predominantly parkinsonian presentation (MSA-P) enjoyed a moderate to excellent response to levodopa initially, although this was unsustainable in most. Almost half of those responsive to levodopa developed drug induced cranial-cervical dystonia. Their facial predilection and their dystonic character, regardless of distribution, seem to distinguish the drug induced dyskinesias of MSA from those seen in Parkinson's disease.

Boesch *et al* do not comment on the discrepancy between the high prevalence of dystonia in their series and the low occurrence rates in prior studies. Undoubtedly the observational meticulousity of the authors of this prospective study played a major role. It is also likely that focal dystonia is overshadowed in most patients by parkinsonism, cerebellar deficits, or corticospinal tract impairment. Nevertheless, Boesch *et al* have

made an important contribution by determining that, if actively sought, dystonia may be one of the most common clinical features of MSA. The authors do note that some doubt was cast on the dystonic nature of antecollis in MSA in a recent report attributing the forward flexion of the neck to myopathy in extensor muscles.⁵

The report of Boesch *et al* helps flesh out our knowledge regarding the clinical repertoire of MSA. It also extends previous descriptions of the response of patients with MSA to levodopa. It is a welcome addition to our expanding body of knowledge on the clinical differential diagnosis of parkinsonism.

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