Editorial

Creutzfeldt-Jakob disease surveillance - Australia at the crossroads?

Creutzfeldt-Jakob disease (CJD) is one of a small number of human neurodegenerative transmissible spongiform encephalopathies (TSEs) which affect people mainly in the 50 to 75 year age range, with a peak incidence in about the mid-sixties. The annual incidence of CJD is approximately one case per million population, and is invariably fatal, usually within a year of onset of symptoms. It usually begins with memory loss, followed by rapidly progressing dementia, loss of coordination, slurred speech and myoclonus, and - in the final stages - akinetic mutism, coma and death. A definitive diagnosis can only be made by histopathological examination of brain tissue, and only in rare cases is a diagnosis confirmed ante-mortem. Other related human TSEs include variant CJD (vCJD), Gerstmann-Sträussler-Sheinker disease (GSS), fatal familial insomnia (FFI), sporadic fatal insomnia and kuru.

It is believed TSEs are caused by the accumulation of an aberrant isoform of a normal cellular protein called a prion (PrP). About 85 per cent of cases of CJD are regarded as sporadic, and are initiated by a rare stochastic change in the secondary structure of one or a few molecules of protein to form the abnormal structure. The aberrant isoform of the PrP is thought to act as a template, causing the normal conformers to switch to the abnormal shape, in a cascade effect. Almost 10 per cent of cases of CJD occur in persons with a family history of the disorder, and the pattern of disease transmission is consistent with an autosomal dominant gene mutation. In most of these families, mutations are found in the gene for the PrP gene. In a very small proportion of patients, CJD is attributable to iatrogenic transmission through neurosurgery or implantation of stereotactic EEG electrodes, or to the administration of cadaver-derived pituitary hormones, or to the use of dura mater or corneal grafts.[1-6] Case control studies have also reported a weak association between surgical treatment and the occurrence of CJD,[7,8] although there have been no confirmed reports of surgical transmission of CJD other than through neurosurgical procedures.

In 1986, bovine spongiform encephalopathy (BSE) was first identified in cattle in the United Kingdom (UK). This disease is characterised by apprehension, aggression and ataxia, with pathological brain lesions similar to those seen in human TSEs. Variant CJD (vCJD) was first reported from the UK in 1996, and to date (28 September 2000) 73 confirmed cases have been reported to the UK National CJD Surveillance Unit.[9] Patients with this condition are typically much younger than those with classical CJD (cCJD), and prominent features include neuropsychiatric and behavioural disorders, and abnormal sensory perceptions. The course of the illness is generally longer than that of cCJD, but is invariably fatal. Spongiform changes

seen in the brain resemble those of kuru more closely than those seen in cCJD. There is now convincing evidence that the vCJD epidemic in the UK has been caused by the consumption of foods contaminated with the BSE agent.[10-13] BSE has never been recorded from Australia, and Commonwealth and State agricultural authorities carry out an active surveillance program.

Although iatrogenic transmission of cCJD has been documented, there is no clinical or epidemiological evidence that the disease is transmissible by blood or blood products. There is, however, concern over the possibility that vCJD may be transmissible by this route, and that circulating lymphocytes may play a role in the pathogenesis of the disease. The recent report of experimental transmission of BSE between sheep by this route[14] is thus of concern. Steps have been taken in the UK to minimise this theoretical risk by undertaking leukodepletion of the blood supply and sourcing all plasma from non-European countries. In contrast to cCJD, the vCJD PrP has been found in the lymphoreticular tissue of all cases of vCJD studied, and in the appendix of an asymptomatic person who developed symptoms of vCJD 8 months later.[15]

Surveillance of human TSEs is conducted by the Australian CJD Registry, which is funded by the Commonwealth Government and is located in the Department of Pathology at The University of Melbourne. CJD is not notifiable, and accurate case ascertainment is largely dependent on voluntary reporting by medical practitioners. Mailouts are posted to neurologists and pathologists semi-annually in an effort to prompt notification of recent or prospective cases. Other methods include searches of death certificates, and review and follow-up of teaching hospital medical records.

Given the unusual presentation of vCJD (with neuro-psychiatric and behavioural changes presenting early in the course of the disease) and the possibility that the vCJD prion may be transmissible through blood, the question arises as to whether current methods of case ascertainment are adequate to detect vCJD ante-mortem, and to protect public health. vCJD has never been recorded in Australia and, based on the UK experience and the rarity of the disease, it is possible that a patient may not be seen by a practitioner with a high index of suspicion early in the course of the illness. A symptomatic or asymptomatic blood donor could continue to donate blood for some time before the diagnosis is considered. Should vCJD be transmissible through the blood supply, there is a clear potential for iatrogenic transmission in this manner. It is for this reason that those visiting Britain for 6 months or more between 1980 and 1996 cannot donate blood in a number of countries (including Australia) and on 30 August 2000 the Canadian authorities, following the second report of vCJD in France,[16] have directed that those visiting France for 6 months or more during that period cannot do so either.[17] The time has now come for enhanced surveillance in Australia of all human TSEs.

Lance Sanders

Principal Scientist, Surveillance and Management Section, Population Health Division, Department of Health and Aged Care, Canberra, ACT.

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