Creutzfeldt-Jakob disease (CJD) after blood product transfusion from a donor with CJD

Article abstract—We report a second case of an association between an albumin transfusion and Creutzfeldt-Jakob disease. On balance, we believe our case represents a chance and not a causal relation.

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Creutzfeldt-Jakob disease (CJD) is a human transmissible spongiform encephalopathy that has iatrogenic (<1 to 5% of cases), sporadic (80 to 90%), and familial (5 to 15%) forms. The transmissible agent appears to be an abnormal isoform of prion protein (PrP) indicated as PrP^{CJD}. Usual physical or chemical methods of decontamination are ineffective.[1] In Canada CJD has an incidence of between 0.6 and 1.1 cases per million population.[2]

Transmission of CJD by transfusion of blood products in humans has not been conclusively demonstrated. We report a case of CJD after an albumin transfusion.

Case report. A 69-year-old man was admitted to the Calgary General Hospital (CGH), Calgary, Alberta, Canada, on March 4, 1996. He had no risk factors for CJD.[3,4]

During triple aortocoronary bypass grafting (August 11, 1994), he received three units of 25% albumin. It was subsequently discovered that all three units were derived from plasma pools that included a donation from a donor later diagnosed with CJD. The donor was aged 57 years when diagnosed. In the spring of 1995, he developed emotional lability, myoclonic jerks, gait abnormalities, and rapidly progressive dementia. Frontal lobe biopsy (July of 1995) showed spongiform encephalopathy, consistent with CJD. An immunoperoxidase stain for PrP^{CJD} was performed (at the University of California Medical Centre, Department of Pathology) using the hydrolytic autoclaving technique and the polyclonal antibody W5512. This showed scattered immunopositive aggregates in the gray matter with some faint, very fine punctate staining more diffusely throughout the neuropil. This plus the microscopic appearance were diagnostic for CJD. Reportedly the donor had given blood on a number of occasions over the years, the last time in April of 1995.

Our patient developed neurologic problems in the spring of 1995 (8 to 10 months post-transfusion) when he became increasingly forgetful. In November of 1995 he wandered from his home and was lost for a number of hours. He moved into a residential facility but could not manage. He was admitted to a local hospital in December of 1995, by which time he had a shuffling gait and stooped posture. Over 3 weeks he became bedridden and lost the ability to feed himself. Four to 5 weeks before his CGH admission he developed myoclonic jerks.

When admitted to CGH, he was lethargic and would only respond to questions by answering "yes" or "no." He could not consistently follow one-stage commands. Myoclonic jerks were noted in both upper extremities. Muscle tone was increased in all four extremities. He could not stand or walk. A diagnosis of probable CJD was made. The patient continued to deteriorate and died on March 31, 1996. An autopsy was performed.

Neuropathologic examination revealed no gross abnormalities. On histologic examination there were prominent vacuolar changes involving all layers of the cerebral cortex (spongiform degeneration), patchy fibrillary gliosis (throughout the cerebral cortex, corpus striatum, thalamus, and dorsal midbrain), and more focal neuronal loss (predominantly in the thalamus). There was minimal involvement of the cerebellum, lower brainstem, and spinal cord. PAS staining failed to identify any kuru-type plaques or other forms of amyloid plaques. In addition there was a focal ischemic lesion in the cerebellum. Immunoperoxidase staining for PrP^{CJD} (done at the University of California Medical Centre, Department of Pathology) showed abundant PrP^{CJD} plaque-like deposits throughout all layers of the cortex with accentuation in the peri-vacuolar spaces. The striatum showed decreased numbers of and smaller-sized plaque-like depositions. The section of the thalamus showed small focal collections of immunopositive material. The levels of PrP^{CJD} deposition correlated closely with the degree of vacuolar change identified on H-E staining.

Genomic DNA was extracted from a sample of frozen spleen, and the PrP gene was sequenced using an ABI automated DNA sequencer. A deletion was noted in the octarepeat region of the gene, which necessitated its cloning into the T/A Cloning vector. One copy of the gene had the normal sequence, and one contained a common 24-base pair deletion within the octarepeat region. This deletion has been reported previously to be a common polymorphism that does not confer genetic predisposition to prion disease.[5] The polymorphic codon 129 genotype was homozygous for methionine.

Discussion. Some researchers have reported the transmission of CJD to animals from buffy coats and whole human blood injected directly into the brain. Albumin for transfusion is prepared by disposing of the cellular elements of blood and heating to 60 °C for 10 hours. This may not be sufficient for protection from CJD transmission.[1] Serum from humans with CJD has not been shown to transmit spongiform encephalopathy to animals, but very few specimens have been tested.[3]

Human transmission of CJD by blood transfusion has never been conclusively shown. A reanalysis of case-control studies of CJD did not suggest any risk

from blood transfusions.[6] Esmonde et al.[7] found that the frequency of blood transfusion or blood donation did not differ in CJD sufferers as compared with matched controls. Heye et al.[8] could not find evidence of transmission of CJD with blood products derived from a donor who died from CJD. Four Australian cases, suggested as being possibly related to blood transfusions, could not be confirmed.[9]

There is one reported case of a possible link with an albumin transfusion.[10] A 57-year-old woman presented with gait problems 2 years after a liver transplant. The liver donor had no known neurologic concerns other than a ruptured cerebral aneurysm (which was the cause of death). An albumin donor had died from probable CJD. This clinical diagnosis was not confirmed by examination of brain tissue. The recipient's diagnosis of CJD was confirmed at autopsy.

The patient we report may have had sporadic CJD. A familial form was ruled out by genetic testing, although he may have been predisposed to CJD because of his homozygosity at codon 129. The association between the transfusion and the development of CJD may have arisen by chance. The albumin transfusion could possibly have led to CJD. Arguments against this would include the shortness of the required incubation period (8 to 10 months) and possibly the clinical features (and pathology) of the patient, which did not suggest a peripheral exposure to the transmissible agent. Even when the transmissible agent was introduced directly into the brain by contaminated instruments, the incubation period was at least 16 months.[3]

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References

1. Goldfarb LG, Brown P. The transmissible spongiform encephalopathies. Annu Rev Med 1995;46:57–65.
2. Stratton E, Ricketts MN, Gully PR. Creutzfeldt-Jakob disease in Canada. Can Commun Dis Rep 1996;22:57–61.
3. Brown P. Environmental causes of human spongiform encephalopathy. In: Baker HF, Ridley RM, eds. Prion diseases. Totowa, NJ: Humana Press, 1996:139–154.
4. Will RG. Epidemiology of Creutzfeldt-Jakob disease. Br Med Bull 1993;49:960–970.
5. Vnencak-Jones CL, Phillips JA. Identification of heterogeneous PrP gene deletions in controls by detection of allele specific heteroduplexes (dash). Am J Hum Genet 1992;50:871–872.
6. Wientjens DPWM, Davanipour Z, Hofman A, et al. Risk factors for Creutzfeldt-Jakob disease: a reanalysis of case-control studies. Neurology 1996;46:1287–1291.
7. Esmonde TFG, Will RG, Slattery JM, et al. Creutzfeldt-Jakob disease and blood transfusion. Lancet 1993;341:205–207.
8. Heye N, Hensen S, Muller N. Creutzfeldt-Jakob disease and blood transfusion. Lancet 1994;343:198–199.
9. Collins S, Masters CL. Iatrogenic and zoonotic Creutzfeldt-Jakob disease: the Australian perspective. Med J Aust 1996; 164:598–602.
10. Créange A, Gray F, Cesaro P, et al. Creutzfeldt-Jakob disease after liver transplantation. Ann Neurol 1995;38:269–272.

Cefuroxime-induced encephalopathy

Article abstract—We describe four patients who developed an encephalopathic syndrome characterized by obtundation or stupor, myoclonic jerks, and asterixis in association with cefuroxime therapy. Three patients had renal failure. These cases suggest that cefuroxime in overdose or in conventional doses in patients with renal failure can cause a reversible encephalopathy. This syndrome may have been unrecognized because it usually occurs in severely ill patients with additional causes for encephalopathy.

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Cephalosporins have been associated with toxic encephalopathic or psychotic reactions.[1,2] Cefuroxime, a widely used second-generation cephalosporin, has been implicated in a case of a psychotic drug reaction.[3] It is most commonly used for community-acquired pneumonia and is administered IV or orally as cefuroxime axetil. The usual IV dose is 750 mg tid, and the oral recommended dose for severe infection is 500 mg bid. Its serum half-life is 1.7 hours, and it reaches CSF concentrations that are approxi-

