J. Comp. Path. 2010, Vol. 142, 27–35

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Pathological Phenotype of Sheep Scrapie After Blood Transfusion

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Summary

Blood transfusion practices have resulted in iatrogenic cases of variant Creutzfeldt–Jakob disease (vCJD) and it is known that sheep blood is also infectious in the pre-clinical stages of natural scrapie and experimentally induced bovine spongiform encephalopathy (BSE). Further investigations have also shown that the pathological phenotype of sheep BSE and human vCJD is maintained after blood transfusion. The present study describes the pathological phenotype, in terms of accumulation of the disease-associated prion protein in brain and lymphoreticular tissues, in sheep receiving blood from donors infected with natural scrapie. The immunohistochemical examinations undertaken showed a degree of phenotypic variability within and between scrapie donors and recipients, which might be attributable to the presence of more than one scrapie strain amongst the donor sheep or to a host adaptation process, or to the interaction of both, rather than to the influence of the route of infection.

Keywords: blood transfusion; immunohistochemistry; prions; scrapie; sheep

Introduction

Transmissible spongiform encephalopathies (TSEs) are neurodegenerative infectious diseases, which include variant Creutzfeldt–Jakob disease (vCJD) in humans, scrapie in sheep and goats, and bovine spongiform encephalopathy (BSE) in cattle. TSEs are characterized by the presence of the disease-associated form of the prion protein (PrP^d) in various tissues; in the brain, the accumulation of PrP^d generally correlates with the appearance of clinical disease, usually after prolonged incubation periods. The presence of PrP^d accumulation throughout lymphoreticular system (LRS) tissues, which is observed in experimental sheep BSE (Foster *et al*., 1996; Jeffrey *et al*., 2001b), in natural scrapie (van Keulen *et al*., 1996; Andreoletti *et al*., 2000; Jeffrey *et al*., 2001a) and in vCJD patients (Hill *et al*., 1999; Wadsworth *et al*., 2001), suggests the possibility that blood could be infectious in these diseases. Descriptions of five transfusion-related vCJD infections have confirmed that this human TSE can be transmitted by blood-derived products (Llewelyn *et al*., 2004; Peden *et al*., 2004; Wroe *et al*., 2006; HPA Press Statement, 2007, 2009).

With the aim of providing information about risk factors of vCJD transmission by blood transfusion, the first transfusion experiments in sheep were established in 1999. The initial results, which showed that BSE could be transmitted from orally infected donors to recipients after a single blood transfusion (Houston *et al*., 2000; Hunter *et al*., 2002), have been confirmed by the final results of the overall experiment, which indicate high transmission rates for both scrapie and BSE (Houston *et al*., 2008). It has also been reported that the pathological phenotype of experimental BSE is not altered after blood transfusion and that this is not dependent on the route of exposure (oral or intravenous) or the nature of the inoculum (brain or blood; Sisó *et al*., 2006), suggesting that a change in the phenotype of vCJD after blood transfusion is unlikely.

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0021-9975/$ - see front matter
doi:10.1016/j.jcpa.2009.06.002

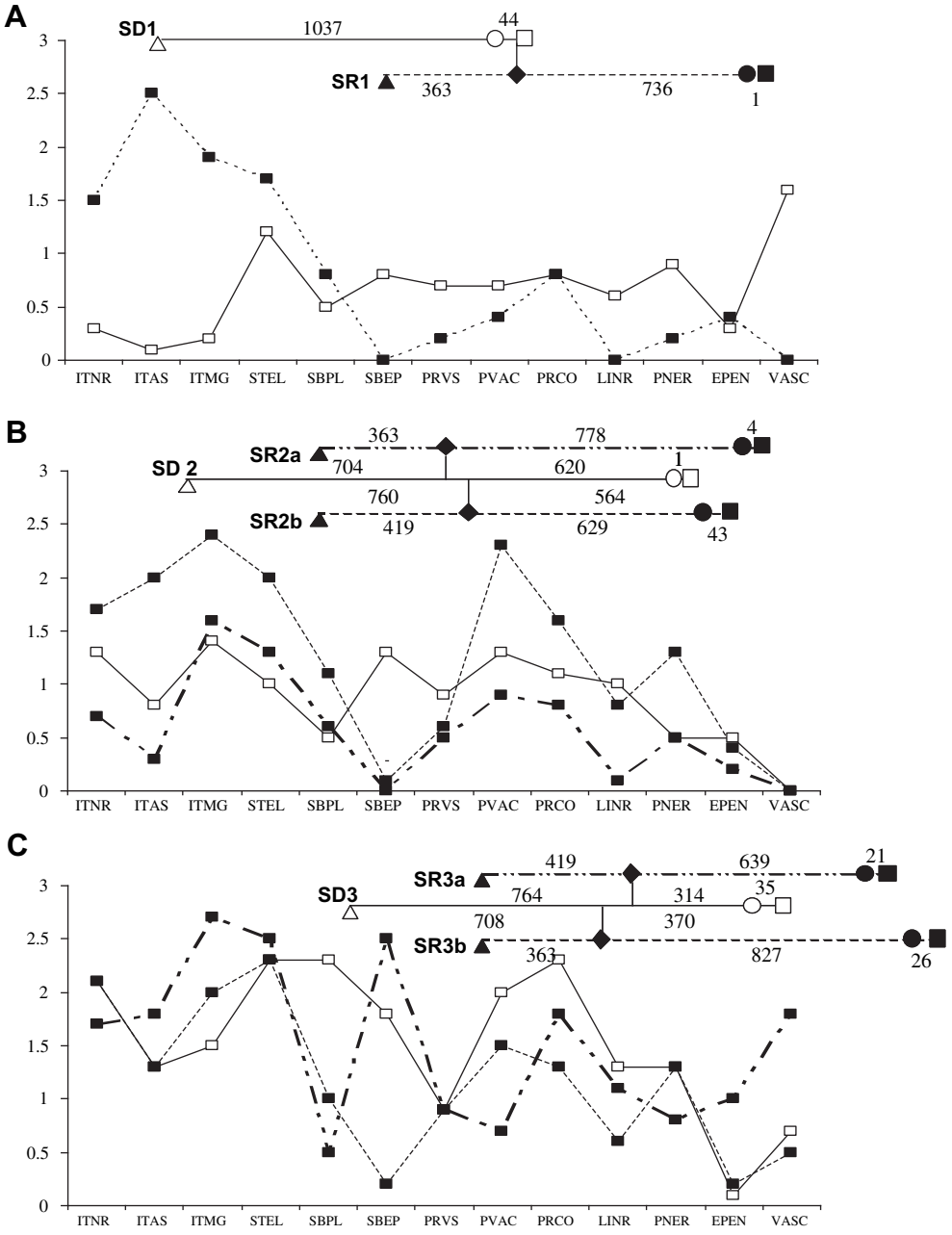

Fig. 1. Individual profiles of PrP^d accumulation in the brains of scrapie donor and recipient sheep. Relationship between donors (D; empty symbols) and recipients (R; solid symbols), indicating points of birth (△ ▲), inoculation (◆), appearance of clinical signs (○ ●) and necropsy (□ ■); numbers indicate days. Donors and recipients in italics are not considered in the estimation of incubation periods or in the average PrP^d profiles of Fig. 2 because they did not show clinical disease. PrP^d types are ITNR, intraneuronal; ITAS, intra-astrocytic; ITMG, intramicroglial; STEL, stellate; SBPL, sub-pial; SBEP, sub-ependymal; PRVS, perivascular; PVAC, perivacuolar; PRCO, particulate-coalescing; LINR, linear; PNER, perineuronal; EPEN, ependymal; VASC, vascular plaques. Donor and recipient sheep identification are detailed here in order to allow traceability of animals between the current paper and that of Houston *et al.*, 2008: SD1 (59 × 28); SD2 (61 × 75,VRQ/ARQ); SD3 (61 × 68); SD4 (59 × 27); SD5 (65 × 02); SD6 (65 × 03); SR1 (F143); SR2a (F149); SR2b (F144); SR3a (F153); SR3b (F152); SR4a (F141); SR4b (F126); SR5a (F310); SR5b (F309); SR6a (F276); SR6b (F277).

The aim of the present study was to extend those observations by determining the phenotype of PrP^d accumulation in tissues from scrapie-infected donors and to compare this with that of recipient animals receiving blood from these donors.

Materials and Methods

Animals and Experimental Procedures

The overall experiment, which included scrapie and BSE blood transfusions, has been described in detail