Teleconference to discuss finding of
vCJD abnormal prion protein in haemophilia patient
14th January 2009

Minutes

Present
CJD Incidents Panel
Mr David Pryer (Chairman)
Dr Pat Hewitt
Prof Don Jeffries
UK Haemophilia Centre Doctors Organisation
Dr Charles Hay
Prof Frank Hill
Department of Health
Ms Jenny Ball
Dr Peter Bennett
Mr Mark Noterman
HPA Secretariat
Dr Nicky Connor
Ms Dominique Brookes
Ms Helen Janecek
Ms Charlotte Mirrielees
Dr Simon Padfield
Dr Akram Zaman

1 Introduction

1.1 The aim of the teleconference was to discuss a paper which Dr Connor had drafted for the forthcoming CJD Incidents Panel meeting on 22nd January. The paper set out the facts of the recently reported case of a haemophiliac patient in whose spleen PrP^{Sc} had been detected at post mortem and posed potential questions to the Panel concerning the implications for the future management of three groups of patients:

- the 14 or more blood donors to the index case
- patients with bleeding disorders
- recipients of medium risk plasma products.

1.2 It was proposed that the paper should be presented at the Panel meeting together with other relevant documents concerning the case. Participants were asked to consider how to take this matter forward.

2 Discussion

2.1 It was extremely important for the case to be described carefully since a single sample from the index patient's spleen had tested positive for PrP^{res} once, the patient had not developed symptoms of vCJD and had died of a non-neurological cause. The National CJD Surveillance Unit had concluded that this patient had an asymptomatic vCJD infection as evidenced by the presence of PrP^{res} in the patient's spleen.

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2.2 The index patient had been treated with Factor VIII including one batch manufactured using plasma donated by a donor who later developed vCJD (TMER 123). The patient had also received blood transfusions from 14 donors since 1998, details of which are available on electronic blood transfusion laboratory records. It was anticipated that searches of the medical records and notes would reveal further blood transfusions before this date, prior to current electronic laboratory records.

2.3 The UKHCDO database had records which accounted for 48% of the batches of plasma products manufactured using plasma from donors who developed vCJD. This incomplete information would affect the precision of any risk assessment produced by the Department of Health HPIH&SD Analytical Team. It would also affect how the UKHCDO and HPA managed and communicated any change in advice.

2.4 In 2005, the Panel had advised the Chief Medical Officer that where one of a group of blood donors to a transfusion recipient who later developed vCJD was known to have developed vCJD, no public health actions needed to be taken in respect of the other donors. In this instance, the donor who had developed vCJD had donated Factor VIII, not blood components. The implications for the blood donors to the patient were less certain.

2.5 Like the previously reported recipient of implicated blood in whose spleen PrP^{res} had also been detected at post-mortem, the index patient was elderly, was MV heterozygous at PrPN gene codon 129 and PrP^{res} had not been detected in CNS tissues. All other spleen samples tested from other haemophilia patients, and 23 other samples from the patient, including three from the spleen, had tested negative for PrP^{res}.

2.6 It was necessary to conduct an analysis of all the possible routes of transmission – plasma product, blood transfusion, surgery and food - to this index haemophilia patient before deciding how likely the Factor VIII was to be the route of transmission.

2.7 It was important to know how many haemophilia recipients had received implicated plasma products, how many had died and their cause of death.

2.8 The TMER study is focussed on individuals who develop CJD. Therefore TMER will not be able to identifythe blood donors to 'at risk' haemophilia patients who die of other causes. The donor (TMER 123) had donated blood on three occasions. All three donations had been used to produce plasma for fractionation: from these donations at least 262 patients with bleeding disorders had been treated with these plasma products were included in the 'at risk' group. In addition, red cell components from the three blood donations had been transfused to three recipients. Two of these recipients had died from non-neurological causes and one is still alive.

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2.9 The issue was raised as to whether chronic hepatitis in haemophilia patients might predispose individuals to acquiring vCJD infection. It is probable that all haemophiliacs who received transfusions before 1986 were exposed to hepatitis C. The index patient had tested hepatitis C antibody and PCR positive.

2.10 The question was asked whether the PrP^{res} detected in the spleen could have been due to sporadic CJD. It was thought that this would be unlikely.

3 Actions to be taken

3.1 It was **agreed** that it was too early to ask the Panel to consider whether it should change its advice on the management of patients who have received implicated plasma products. More work was needed before the impact of this case on Panel advice could be properly evaluated. In particular, it was vital to be clear about the meaning of the observation of PrP^{res} in the index patient and the significance of this for patients with bleeding disorders and the 14+ donors to the index patient.

3.2 As a result of the umbrella approach to the management of patients with bleeding disorders who had received UK-sourced clotting factors between 1980 and 2001, public health precautions had already been put in place.

3.3 It would be necessary to ascertain the index patient's surgical history. If the Panel decided that the status of the index patient was 'at risk of vCJD for public health purposes and presumed infected' surgical contacts would need to be traced, contacted and informed that they were at risk of vCJD for public health purposes. Prof Hill **agreed** to ask the local clinician, with the support of the local CCDC, to ascertain the index patient's full surgical history which was likely to be extensive.

3.4 Although the Western blot test result clearly indicated vCJD, given the importance of the case, it was **agreed** that Prof James Ironside would be asked to comment on the probability of the presence of PrP^{res} being due to sporadic rather than variant CJD.

3.5 In due course, there would need to be a joint letter from the UKHCDO and the HPA to all haemophilia centre doctors (prior to the publication of any paper on the case) explaining the significance of the case and asking them to inform (using wording provided by the UKHCDO and the HPA) their patients. The 62 patients who had received the same batch of Factor VIII derived from TMER 123 as the index case would need especially carefully constructed information. It was felt that there was unlikely to be a leak in the near future since the case had already been known about by a small group of people and the patient's family for about 2 months. It would be vital to publish a paper once the implications of the case had been agreed by the relevant organisations. It was **agreed** that all messages concerning the case should

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clearly communicate the uncertainties in its interpretation as investigations and data collection were ongoing.

3.6 The UKHCDO, with the help of the NBS and the HPA, was consolidating the various streams of information about patients, batches and doses on the UKHCDO database and filling in information gaps to enable further analysis, for example, by age and dosage.

3.7 There were two problems concerning the immediate management of the 14+ donors to the index case. The first was the fact that they may still be donors and the second that their deaths would not be notified to the TMER unless they developed CJD. In view of the possible transmission of vCJD to this haemophilia patient and the ongoing investigation, it would be wise for NHSBT to prevent the issue of any blood components from the identified donors for a short period, without notification of the donors at this stage. This would be the usual immediate action on first notification of a case of possible transfusion-related infection, and NHSBT would take this action on the advice of those present. It was **agreed** that this should be done.

3.8 It was **agreed** that further work should be done on finding information in the following areas to assist the HPIH&SD Analytical Team in preparing a paper for the Panel meeting on 20th May:

- The number of deaths and main causes of death for haemophiliacs.
- Obtaining missing data, where available, on haemophilia patients from UKHCDO colleagues. A special meeting of the UKHCDO executive group might have to be organised to facilitate its collection.
- In relation to the index patient:
    - an assessment of the most likely route of transmission of the vCJD infectivity
    - a full history of all the blood and plasma products with which they were treateed
    - an investigation of the surgical history.

3.9 It was **agreed** that the HPA Secretariat would circulate a draft letter for haemophilia doctors to be circulated to Dr Hay and Prof Hill for comment.

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