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APPENDIX BHaemophilia Centre Directors' AIDS InvestigationSurveillance of AIDS cases in patients with blood coagulation disordersUpdate - 10.9.83

Case A/1, the first patient notified to the Oxford Haemophilia Centre as a possible case of AIDS remains in reasonable health. In July 1983 he suffered from a moderately severe attack of herpes labialis, which responded to treatment with acyclovir, but no other complications have occurred.

Case A/4, a mild haemophiliac (VIIIc 2%) aged 57 was for many years maintained on cryoprecipitate. He also received one batch of NHS (Lister) factor VIII in 1976 and a second in 1978, but had never received factor VIII made from plasma originating in the USA.

In December 1981, he underwent a herniorrhaphy operation and was transfused with 3 batches of factor VIII made from US plasma (30,000; 10,188; and 1896 factor VIII units per batch respectively). He contracted Non-A, non-B hepatitis 3 weeks later and was found to be hepatitis B surface antigen (HBsAg) positive in September 1982. He has remained a hepatitis B'e' antigen (HBeAg) positive carrier ever since. He was noted to have an enlarged liver in February 1982. This persisted until June 1982 and was possibly related to his non-A, non-B hepatitis. He had no lymphadenopathy or other feature of this syndrome. He showed some serological evidence of reactivation of EB virus infection in September 1982. From June 1982 he suffered from severe malaise and over the next year suffered from 3 bouts of undiagnosed fever. He contracted oral candidiasis in May 1983 and varicella-zoster infection of the right arm one month later. These resolved with appropriate treatment.

Laboratory investigations in May 1983 revealed Hb 12.7 G%; w.b.c. $3.0 \times 10^3/\text{cu mm}$; lymphocytes $0.98 \times 10^3/\text{cu mm}$; T cells $0.52 \times 10^3/\text{cu mm}$; T-helper cells $0.07 \times 10^3/\text{cu mm}$; T-suppressor cells $0.43 \times 10^3/\text{cu mm}$; T-helper/suppressor ratio 0.16. There was thus a significant reduction in T-helper cells.

This case was considered to be a mild or prodromal case of AIDS. The degree of depression of cell mediated immunity (CMI) was more than would be expected in a case of chronic hepatitis B, which usually show a T-helper/suppressor ratio of less than 1.0 due to an increase in the T-suppressor cells (Dr. Dale Lawrence CDC Atlanta - personal communication).

The CMV antibody titre was 1/16; herpes simplex 1/24 (both by CFT). The antibody to Pneumocystis carinii was 1/8 on 9.5.83. The immunofluorescence titre to EB virus capsid antigen rose from 1/128 on 15.12.81 to 1024 on 1.9.82.

He remained unwell through June and July 1983 and his health deteriorated and he died on or about August 23 1983. He was noted to have signs of pneumonia just before he died and Pneumocystis

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carinii infection was suspected clinically. Preliminary results of a post mortem have confirmed the presence of Pneumocystis carinii pneumonia, and this has now been confirmed histologically. There was also acute tubular necrosis of the kidneys. No other opportunistic infections or tumours were found.

Full clinical details and the epidemiological background to the case are not yet available, but as the patient was not a drug addict or a homosexual, this must be investigated as the first confirmed case of AIDS possibly associated with transfusion of blood products in the UK.

Proposed Follow-up of Factor VIII of US origin transfused to cases A/1 and A/4

Nine suspect batches of factor VIII transfused to case A/1 between 1.1.80 and 1.3.83 will be followed up. Haemophilia Centres have already been sent forms to be completed so that a register of patients who have received these batches can be completed. The detailed protocol for the follow-up is given in the enclosed paper AIDS/7. The additional three batches associated with case A/4 will be followed up in the same way as those related to case A/1. The batches associated with each case are different and therefore each may constitute a separate 'transfusion event'.

So far, 13 Haemophilia Centres who used the batches of factor VIII associated with case A/1 have completed returns showing the patients transfused with these batches. All Haemophilia Centres were circularised in this survey and this has meant that many Centres had to make a nil return. Through the co-operation of the manufacturers I have obtained complete lists of the distribution of each batch associated with case A/1. This has revealed that a few bottles of factor VIII were sent to hospitals not registered at Oxford as Haemophilia Centres. In future only Centres who received the relevant batches will be contacted. Checks will be made with the manufacturers of the concentrate associated with case A/1 to see if any hospitals or other practitioners who used these batches have been missed.

Other cases reported in the AIDS survey

Three patients with autoimmune type thrombocytopenia have been reported. We propose to conduct a small survey to identify cases of this condition which have occurred in haemophiliacs since 1.1.80 to see if there has been an increase in this condition related to AIDS.

One patient with generalised lymphadenopathy has also been reported. His full transfusion history is not yet available.

Hepatitis B 'e' antigen positive carriers as a marker for immunosuppression in haemophiliacs

Case A/4 became HBeAg positive during the course of his illness. We have received reports that 4 other patients who contracted hepatitis B last year are still HBeAg positive carriers. Investigations will be carried out to see if this has any relation to the AIDS cases reported in this survey.

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*to follow