# Letters to the Editor

## FATAL AIDS IN A HAEMOPHILIAC IN THE UK

SIR,—Hitherto the most serious infection to which haemophiliacs given clotting factor concentrates were thought to be at risk was hepatitis B, but now attention has focused on acquired immunodeficiency syndrome (AIDS), following reports of fifteen cases of *Pneumocystis carinii* pneumonia in haemophiliacs in the United States.[1-3] No definite case of AIDS in a haemophiliac has yet been reported in Britain although one patient may have early features of the syndrome.[4] We report here a fatal case of AIDS in a haemophiliac who received intensive treatment with factor VIII (FVIII) concentrate of US origin.

An otherwise fit 55-year-old heterosexual man with haemophilia A (FVIII 2%) underwent an inguinal herniorrhaphy in December, 1981, under cover with lyophilised FVIII concentrate. He received 48 253 IU of commercial FVIII concentrate of US origin over 12 days. This was his first exposure to commercial FVIII concentrate. Since 1973 he had received an average of 5000 IU of FVIII per year in the form of cryoprecipitate and concentrate (Blood Products Laboratory, Elstree).

In January, 1982, he was admitted to hospital with pyrexia and he was found to be vague, forgetful, irritable, and confused. Investigations (table I) revealed lymphocyte count of $5 \cdot 1 \times 10^9$/l with many atypical lymphocytes and a raised aspartate aminotransferase (AST) and serum bilirubin. He was HBsAg negative and tests for influenza, legionnaires' disease, toxoplasmosis, mycoplasma pneumonia, cytomegalovirus, and Epstein-Barr virus were negative. A CT scan of the brain and CSF examination were normal. In February, 1982, he was still unwell, lethargic and irritable and occasionally confused. Hepatomegaly developed and the lymphocytosis persisted. He remained HBsAg negative and non-A, non-B hepatitis was diagnosed.

TABLE I—SELECTED LABORATORY DATA

| Date | WBC ($\times 10^9$/l) | Lymphocytes ($\times 10^9$/l) | Neutrophils ($\times 10^9$/l) | Atypical lymphocytes | Liver function (AST, IU/l) |
|---|---|---|---|---|---|
| January, 1982 | 8·8 | 5·1 | 3·5 | + | 23 |
| August, 1982 | 3·4 | 1·9 | 0·6 | + | 21 |
| October, 1982 | 3·2 | 0·9 | 1·7 | | 17 |
| April, 1983 | 3·1 | 0·8 | 1·7 | + | 13 |
| May, 1983 | 3·0 | 1·2 | 1·5 | + | 13 |
| August, 1983 | 5·1 | 0·4 | 4·4 | | 30 |

In March, 1982, he presented with herpes zoster of the right arm, the lesion resolving spontaneously. By July, 1982, he had improved (no hepatomegaly, AST still raised) but in August he again felt unwell, lethargic, and listless. In October he presented with an intradermal haematoma of the left ring finger, which was excised under cryoprecipitate cover. He was by then HBsAg positive. He had received no FVIII since December, 1981. Liver function tests were normal.

In February, 1983, he was admitted with an iliopsoas bleed. He was given 44 800 IU of cryoprecipitate and 16 000 units of FVIII concentrate (Blood Products Laboratory). He had become a HbsAg and HbeAg carrier and remained so until his death. In April, 1983, he was admitted with a left quadriceps haematoma and was treated with cryoprecipitate and FVIII concentrate (Blood Products Laboratory). The haematoma resolved over 2 weeks.

In May herpes labialis and oral candidiasis responded to idoxuridine and nystatin. At this time the spleen tip was palpable. Candida infections of the perineum and groin responded to topical nystatin. A perineal rash from which *Epidermophyton floccosum* was isolated responded to topical miconazole.

At this time AIDS was suspected. IgA and IgG levels were raised. T cell studies supported the diagnosis (table II).

TABLE II—IMMUNOLOGICAL EVALUATION (MAY, 1983)

| | Patient | Normal range |
|---|---|---|
| *Immunoglobulins (g/l)* | | |
| IgG | 24·0 | 5–14 |
| IgA | 14·0 | 0·5–2·5 |
| IgM | 1·5 | 0·5–2·0 |
| *T cells ($\times 10^9$/l)* | | |
| Peripheral (OKT 3) | 0·47 | 0·83–2·44 |
| Helper (OKT 4) | 0·07 | 0·54–1·59 |
| Suppressor (OKT 8) | 0·43 | 0·29–0·86 |
| *Helper/suppressor ratio* | 0·16 | 1·4–2·5 |

In August, 1983, he complained of intermittent fever, chills, dry cough, and dyspnoea on exertion. He had oral candidiasis. There was no lymphadenopathy, local chest signs, or hepatosplenomegaly and the fundi were normal. A chest X-ray showed diffuse interstitial infiltration, and *P carinii* pneumonia was suspected but serological tests were negative. *Aspergillus fumigatus* serology was weakly positive. Although bronchoscopy with alveolar lavage, bronchial brushings, and biopsy yielded no evidence for pneumocystis infection, the clinical picture was so suggestive that he was treated with high dose co-trimoxazole. His temperature settled within 3 days but he became uraemic and oliguric, so the co-trimoxazole was discontinued. He deteriorated and the pulmonary lesion worsened. Treatment with pentamidine was started but he became pancytopenic and died 2 days later.

Necropsy revealed no gross macroscopic abnormalities other than oedematous lungs and atrophied lymph glands. Histological examination of the lungs revealed extensive infiltration by *P carinii*. The liver was normal apart from some mild fibrosis and without evidence of cirrhosis.

The diagnosis of AIDS is essentially clinical but our patient met the Centers for Disease Control's criteria[5] in that, without any known cause for immunodeficiency, he had *P carinii* pneumonia. Immunological abnormalities in AIDS include hypergammaglobulinaemia and reversed helper/suppressor T-cell ratios due to a reduction in absolute number of helper cells. Abnormalities of T cell subsets have been described in patients with haemophilia without evidence of AIDS but the reversed T cell ratio has usually been due to an increase in suppressor cell numbers while in our patient the low ratio was due to an absolute reduction in T helper cells with normal numbers of suppressor cells. Although similar reduced helper/suppressor ratios have also been described in hepatitis B infection[6] they have usually been transient and have not been described in carriers.

Our patient became unwell (and remained so until his death 18 months later) a few weeks after receiving treatment with a large volume of commercial FVIII concentrate of North American origin over a short period of time. This was his first exposure to a commercial product. It seems highly probable that the development of AIDS (and hepatitis B and non-A, non-B hepatitis) was related to this treatment. This case provides further evidence[1-3,7] for a link between exposure to blood products and AIDS.

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