HTLV-III INFECTION ASSOCIATED WITH GLANDULAR-FEVER-LIKE ILLNESS IN A HAEMOPHILIAC

SIR,—Although there is evidence of a rapid increase in the prevalence of antibodies to HTLV-III/LAV in "at risk" groups[1,2] most infections are asymptomatic. A report of needlestick transmission of HTLV-III[3] prompted us to record a severe glandular-fever-like illness in a haemophiliac given factor VIII (FVIII) cover for synovectomy.

This 14-year-old boy underwent a left knee synovectomy because recurrent severe haemarthroses had not responded to medical management. FVIII replacement was with Scottish National Blood Transfusion Service intermediate purity concentrate; he had never received any commercial blood products. The operation and first postoperative week were uneventful, but then the knee became swollen and painful and the bloodstained discharge showed evidence of infection (see figure). The symptoms settled on antibiotic therapy but then recurred, and the continued discharge of bloodstained fluid led to surgical exploration with removal of blood clots of varying ages and evidence for the two organisms found in the discharge. A week later the patient became very toxic and feverish; *Escherichia coli* was isolated from his urine and the knee became painfully swollen again. A third operation with careful debridement followed by irrigation of the joint cavity was required. By the time the patient had recovered from this episode he was malnourished. After 2 weeks of dietary supplementation by nasogastric feeding he made a steady clinical recovery.

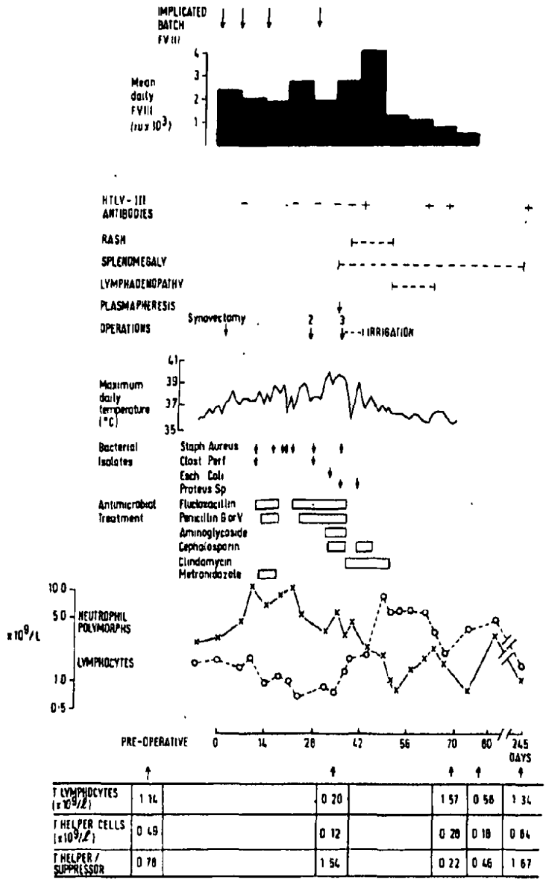
On the day before the knee was explored for the third time he had a 1 litre plasmapheresis both because of in-vitro evidence (not confirmed later) of inhibition of phagocytic function by a plasma factor and in an attempt to counter the large amounts of fibrinogen infused with the intermediate purity FVIII over the previous 33 days. FVIII replacement for the 2 weeks after plasmapheresis was with a high purity commercial product and thereafter NHS FVIII was given.

Around the time of the third operation, 5 weeks after the synovectomy, the patient had a macular rash and splenomegaly, and, 2 weeks later, generalised lymphadenopathy. There was no evidence of infection or reactivation with cytomegalovirus, Epstein-Barr virus, hepatitis B virus, influenza virus, adenovirus, respiratory syncitial virus, mumps, herpes simplex, or rubella viruses, parvovirus, *Brucella, Leptospira, Chlamydia,* Q fever, *Mycoplasma pneumoniae,* or *Toxoplasma.* Stored sera were retrospectively tested for antibodies to HTLV-III and were positive for the first time 44 days after synovectomy (see figure).

Neutrophil polymorph, lymphocyte, T lymphocyte, and T helper cell numbers and T helper/suppressor ratio are illustrated in the figure. Many of the circulating cells resembled very large reactive lymphocytes, some with irregular nuclei with nucleoli and deeply basophilic cytoplasm. The platelet count fell from normal to 90×10^9/l with a nadir a month after the final operation.

Wound sepsis after synovectomy is very rare and its development may reflect transient immunosuppression. At no stage was pus observed, either leaking from the wound or at the two post-synovectomy explorations; nor was an appropriate neutrophilia observed in the blood, and the lymphocyte count started to rise following the plasmapheresis and third operation, suggesting that a circulating factor may have caused the lymphopenia (see figure).

The rash, lymphadenopathy, and splenomegaly are consistent with a viral infection and seroconversion to anti-HTLV-III positivity at that time supports our view that this virus was the cause. The clinical features resemble those in the needlestick incident[3] and a case in which blood transfusion resulted in a postoperative "mononucleosis-like illness" before AIDS developed.[4] HTLV-III infection was associated with an acute temporary reduction in T-helper cell numbers and T helper/suppressor ratio, but these indices returned to normal within a few months. This is similar to the pattern of LAV infection of chimpanzees.[5] The clinical immunosuppression and lack of appropriate leucocytosis may have resulted from this viral infection. Postoperatively the patient received 54 vials (about 13 000 IU) of Scottish National Blood Transfusion Service FVIII, which has lately been suspected of causing HTLV-III seroconversion in a further fourteen haemophiliacs (unpublished).



Clinical course, HTLV-III antibody status, and lymphocyte counts in haemophiliac with infective complications after synovectomy.

The patient is clinically well 8 months after his operation; despite the postoperative haemarthroses and repeated surgery he has lost no extension and can flex the knee to 90°. During this time he has had no bleeds into this joint or elsewhere. He continues to have a mild neutropenia (total leucocytes $1\cdot7\times10^9$/l, lymphocytes $1\cdot2\times10^9$/l) and 2 cm splenomegaly.

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1 Melbye M, Biggar RJ, Chermann JC, et al. High prevalence of lymphadenopathy associated virus (LAV) in European haemophiliacs. *Lancet* 1984, ii: 40–41.
2. Cheingsong-Popov R, Weiss RA, Dalgleish A, et al. Prevalence of antibody to human T-lymphotropic virus type III in AIDS and AIDS-risk patients in Britain. *Lancet* 1984; ii: 477–80.
3 Editorial. Needle-stick transmission of HTLV-III from a patient infected in Africa. *Lancet* 1984, ii: 1376–77.
4 Feorino PM, Kelyenaraman VS, Haverkos HW, et al. Lymphadenopathy-associated virus infection of a blood donor/recipient pair with AIDS. *Science* 1984, 225: 69–72.
5. Francis DP, Feorino PM, Broderson JR, et al. Infection of chimpanzees with lymphadenopathy-associated virus. *Lancet* 1984; ii: 1276–77.