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Comments

United Kingdom

Oesophageal Candidiasis in an HIV-Negative Individual Treated with Factor VIII Concentrate

Sir,

A variety of abnormalities have been observed in the immune systems of HIV-negative haemophiliacs who have been treated with pooled blood products (1, 2). There is, however, controversy about the clinical significance of these observations (3), and few reports of overt morbidity (4). We report a case of oesophageal candidiasis, a condition strongly suggestive of immune dysfunction, in an HIV-negative patient treated with factor VIII concentrate and with evidence of lymphocyte activation as described in similarly treated patients (2) but with no other predisposing factors for developing this condition.

A 73-year-old woman with type 1 von Willebrands disease presented with melaena and resultant anaemia. In view of her previous history of severe gastro-intestinal bleeding from colonic angiodysplasia responding poorly to treatment with cryoprecipitate alone, she was treated with BPL 8Y concentrate. Over the ensuing 6 days she received a total of 10,000 units of factor VIII concentrate and 2 units of red cells with a satisfactory clinical and laboratory response. On day 8 she received a further single dose of 1,500 units of factor VIII in order to cover upper gastrointestinal endoscopy and possible biopsy. At endoscopy scattered white patches of candidiasis were seen throughout the oesophagus; in addition superficial gastritis was noted. Microscopic examination of biopsy specimens confirmed a mild chronic gastritis and an oesophageal inflammatory cell infiltrate with numerous candida in the epithelium. The patient was successfully treated with oral fluconazole for 1 month.

Our patient had first been treated with cryoprecipitate in 1981 and was first exposed to factor VIII in 1988 when she received 28,240 units of intermediate purity concentrate along with a further 426 units of cryoprecipitate. From 1989 until her recent presentation she received a total of 2,239 units of cryoprecipitate but no further factor VIII.

Tests for HIV antibody were persistently negative both before and after the development of oesophageal candidiasis. She had no evidence of previous infection with hepatitis B virus (anti HBc negative, HBsAg negative), but had detectable antibodies against hepatitis C virus by second generation ELISA. Review of T-cell subsets showed normal values for CD4, CD8 cells and CD4/CD8 ratio 6 weeks before (780×10^6, 410×10^6 and 1.9 respectively) and 11 weeks after the diagnosis of oesophageal candidiasis (570×10^6, 280×10^6 and 2.0), however, percentages of activated T-cells (DR+ve) were elevated at both time points (11 and 8%: n <5%). Markedly raised levels of beta-2 microglobulin (5.2 mg/l, n <2.5 mg/l), and soluble interleukin 2 receptors (2,300 u/l, n <400 u/l), provided further evidence of lymphocyte activation. Cell mediated immunity as tested by skin recall antigens (Multitest, Merieux), was normal with a positive response to 3 of 7 antigens.

Oesophageal candidiasis is a disorder usually seen in the setting of severe immunocompromise, as in patients with AIDS and in patients receiving high dose chemo-radiotherapy for malignant conditions. Its occurrence, therefore, in an HIV-negative patient with none of the associated risk factors is notable particularly in view of the on going concern regarding the possible immunosuppressive effects of blood products.

It is noteworthy that our patient had no quantitative abnormality of lymphocyte subsets and had normal cell mediated immunity to recall antigens. The cause and significance of alteration of immunological parameters in HIV-negative haemophiliacs and particularly their relationship to infection with hepatotropic viruses and product purity remains unclear. Concern has been expressed regarding increased rates of infection and progression of chronic liver disease in haemophiliacs, and the possible contributing effect of infusions of factor VIII to these observations. There is, however, as yet a paucity of evidence to substantiate these suspicions.

Whilst the evidence of lymphocyte activation seen in this patient alone does not indicate immunodeficiency, the occurrence of oesophagel candidiasis is very rare in individuals with normal immune systems. We feel that this report gives further cause for concern that pooled blood products may lead to clinically significant immune suppression.

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