# SHORT REPORTS

## A new manifestation of infection with Epstein-Barr virus

We describe a patient with a specific T-lymphocyte defect in whom Epstein-Barr (EB) virus produced a prolonged bizarre illness which responded to treatment with corticosteroids.

### Case report

A 27-year-old English housewife was admitted to the Lister Unit, Northwick Park Hospital, on 1 March 1977 with a 10-day history of fever, sweating, rigors, and sore throat. She had received ampicillin without improvement. History included glomerulonephritis when she was 11, very severe chickenpox lasting two months when she was 13, and severe oral herpes complicated by a facial nerve palsy when she was 24. She had also suffered measles, rubella, and mumps but these were mild illnesses. There were no recorded episodes of severe bacterial infections. Family history was non-contributory.

She was ill with a temperature of 38·5°C and diffuse erythema of face (not typical of lupus erythematosus or the ampicillin-mononucleosis eruption). Lymph nodes were palpable in cervical, inguinal, and axillary regions; the spleen was palpated 2-3 cm below the left costal margin. There was no tonsillar exudate but a few petechiae were present on the palate. The tongue was smooth and inflamed. A minor degree of proteinuria was noted. No abnormality was found in other systems. Blood pressure was 120/80 mm Hg.

Initial laboratory results showed: haemoglobin 11·0 g/dl, leucocytes $7·9 \times 10^9$/l, 64% neutrophils, 31% lymphocytes, 4% monocytes, 1% eosinophils, with no atypical mononuclear cells; erythrocyte sedimentation rate (ESR) 70 mm in 1 h. Paul-Bunnell test positive (1/80 before absorption; 1/80 after absorption with guinea-pig antigen; nil after absorption with ox red cell antigen). This weakly positive reaction persisted during the acute phase of illness. Serum bilirubin concentration was 24 μmol/l (1·4 mg/100 ml), serum aspartate aminotransferase 108 IU/l. Urine was sterile on culture with a few red blood cells and white blood cells. Because of the possibility of streptococcal infection she received intramuscular penicillin for one week.

High swinging fever continued; pallor and ascites were noted, but no oedema was present. Haemoglobin fell to 8·7 g/dl; there was a positive reaction on the direct Coombs test with anti-i antibody. Antibodies to EB virus capsid antigen (indirect immunofluorescence) showed a progressive rise from a titre of 1/5 (on 4 March, the third hospital day), 1/5 (14 March), 1/20 (26 July), to 1/40 (13 September). Toxoplasma dye test repeatedly gave negative results. EB virus IgG was 1/512 on 9 March and 1/256 on 26 July, when IgM was 1/8. Titres against cytomegalovirus (CMV) were: complement fixation test, 1/1024 on 28 March and 1/128 on 26 July; IgM, 1/32 on 28 March and 1/2 on 26 July. Many laboratory values were normal, including serum immunoglobulin concentrations, repeated blood cultures, antistreptolysin O titres, tests for lupus erythematosus, bone marrow examination, and extensive serological tests for viruses other than CMV and EB virus. CMV was not cultured from the urine.

On 14 March prednisolone 30 mg/day was administered; her temperature returned towards normal but recurred with rigors on 21 March, when the steroid dose was doubled. Thereafter, by slow reduction in dose, fever and anaemia were controlled. Corticosteroids were discontinued after three months. The patient was discharged on 17 May and was last seen on 25 October 1977, when she was well with a normal blood count, negative Paul-Bunnell test, and normal ESR.

*Immunological studies*—Cytotoxicity tests against a lymphoblastoid cell line expressing Epstein-Barr viral surface antigen were performed on seven separate samples during the illness.[1] Lymphocytes consistently failed to produce specific cytotoxicity for CLA 4 cells, whereas the mononuclear cells from two patients with characteristic atypical mononuclear cells gave the expected response (see table). The following T-lymphocytes functions were normal: E-rosette formation, helper function in Ig synthesis, response to phytomitogens, and interferon production.

*Cytotoxicity for lymphoblastoid cells*

| Cell donor (No of experiments) | Mean (±SD) cytotoxicity (%) | | |
|---|---|---|---|
| | Normal serum | | Patient's serum (PHA absent) |
| | PHA absent | PHA present | |
| Patient (7) | 2·4±1·8 | 10·7±6·2 | 12·9±9·2 |
| Patients with infectious mononucleosis (2) | 13·5±0·3 | 14·2±1·2 | 12·2±12·3 |
| Normal controls (7) | 4·9±2·4 | 13·6±3·5 | 11·0±2·7 |
| Function tested | Specific T-cell cytotoxicity | Non-specific T-cell cytotoxicity | K-cell cytotoxicity |

$^{51}$Cr release from CLA 4 cells with 10:1 ratio of effector:target cells after 18 hours' incubation. Background release was 23·6±2·6%.

### Comment

The rise in capsid antibody is accepted as evidence of primary EB virus infection; the behaviour of the CMV antibody titres was most probably an anamnestic response.

We suggest that our patient suffered from a specific defect in cell-mediated immunity to EB virus, which was shown morphologically in her failure to produce atypical mononuclear cells and functionally in her ability to mount a specific reaction against cells infected by this agent. Her history of severe varicella indicates that there was a constitutional inability to react to DNA containing herpes viruses.

Manifestations of EB virus infection range from asymptomatic seroconversion and typical infectious mononucleosis to African Burkitt's lymphoma and probably nasopharyngeal carcinoma.[2] The virus has also been implicated in two other lymphoproliferative disorders.[3 4] Our patient's illness was intermediate in severity and outcome between common self-limiting infectious mononucleosis and the more aggressive malignant condition associated with the virus.

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[1] Denman, A M, and Pelton, B K, *Clinical and Experimental Immunology*, 1974, **18**, 13.
[2] Epstein, M A, and Achong, B G, *Lancet*, 1973, **2**, 836.
[3] Bar, R S, *et al*, *New England Journal of Medicine*, 1974, **290**, 363.
[4] Purtilo, D T, Cassel, C, and Yang, J P S, *New England Journal of Medicine*, 1974, **291**, 736.

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## Alcohol-induced pain in secondary syphilis

Pain at the site of disease after drinking alcohol is well known in Hodgkin's disease.[1 2] It has also been reported in carcinoma of the cervix and bronchus and rarely in other neoplasms,[3] though in few infective conditions—Alexander[4] reporting it in osteomyelitis and Conn[5] in pyogenic lymphadenitis. No reference could be found to its association with syphilis, and I report such a case.

### Case report

An 18-year-old woman was sent to the special clinic at Loughborough General Hospital by her GP because of a generalised rash. The rash had been present for three weeks and was non-irritant. She said that she had pain and swelling in her neck when she drank alcohol. The pain came on almost immediately after taking any form of alcohol, even cider, and was so severe that she had given up drinking alcohol; some residual discomfort remained for up to two days afterwards.

She had a pityriasiform rash on the trunk and arms. There was bilateral lymphadenopathy in the anterior and posterior triangles of the neck and inguinal lymphadenopathy. She also had extensive vulval warts and trichomonal vaginitis. The results of routine serological tests for syphilis were all positive (WR 20 units; and RPCFT, VDRL, TPHA, and FTA (ABS)). The white cell count was $8·6 \times 10^9$/l with 37% neutrophils, 51% lymphocytes, 6% monocytes, and 6% eosinophils. An occasional atypical lymphocyte was reported on the film but the result of a specific test for glandular fever was negative.