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-mono-nucleosis 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 $24 \mu\text{mol/l}$ (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-lymphocyte functions were normal: E-rosette formation, helper function in Ig synthesis, response to phytohemagglutinin, and interferon production.

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.

We thank Dr R N P Sutton of the Public Health Laboratory, Manchester, for kindly estimating capsid antibodies in this patient.

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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—Alexander⁴ reporting it in osteomyelitis and Conn⁵ 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 pityriasisiform 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.

Cytotoxicity for lymphoblastoid cells

Cell donor (No of experiments)	Mean ($\pm$ SD) cytotoxicity (%)		
	Normal serum		Patient's serum (PHA absent)
	PHA absent	PHA present	
Patient (7)	2.4 $\pm$ 1.8	10.7 $\pm$ 6.2	12.9 $\pm$ 9.2
Patients with infectious mononucleosis (2)	13.5 $\pm$ 0.3	14.2 $\pm$ 1.2	12.2 $\pm$ 12.3
Normal controls (7)	4.9 $\pm$ 2.4	13.6 $\pm$ 3.5	11.0 $\pm$ 2.7
Function tested	Specific T-cell cytotoxicity	Non-specific T-cell cytotoxicity	K-cell cytotoxicity

¹Cr release from CLA 4 cells with 10:1 ratio of effector:target cells after 18 hours' incubation. Background release was $23.6 \pm 2.6\%$.

She was treated with Triplopen (benethamine and procaine penicillin with benzyl penicillin sodium) 1.2 megaunits intramuscularly daily for ten days. Two weeks after treatment she could drink alcohol without adverse effect. The lymphadenopathy resolved within three weeks. At six months her Wassermann test result was negative and she had had no recurrence of the pain with alcohol. Her regular consort was treated for early latent syphilis but had no history of alcohol-induced pain.

Comment

The cause of alcohol-induced pain is not known. Brewin³ has suggested acute vasocongestion and in this case the patient complained of swelling of the neck associated with the pain. It seems unlikely that it is related to the infecting organism as her consort, who was the source of the infection, had no similar symptom. Conn⁵ described the prompt relief of symptoms when the condition was due to an infection once this had been cured as happened in this case.

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² James, A H, *Quarterly Journal of Medicine*, 1960, **29**, 47.

³ Brewin, T B, *British Medical Journal*, 1966, **2**, 437.

⁴ Alexander, D A, *British Medical Journal*, 1953, **2**, 1376.

⁵ Conn, H O, *Archives of Internal Medicine*, 1957, **100**, 241.

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Improved method of transvenous liver biopsy

The transvenous approach to liver biopsy described by Rösch *et al* in 1973 was found to be safe and successful in obtaining biopsy specimens for histological examination in patients with an increased bleeding tendency.¹ The technique has not been widely adopted, however, because the procedure is technically difficult and because the specimens compare unfavourably in size with those obtained when a modified Vim-Silverman Trucut (Travenol Laboratories Inc, USA) percutaneous biopsy needle has been used.² We report a new transvenous needle which overcomes some of these problems.

Description, method, and results

The prototype needle was constructed from flexible endoscopy forceps (Olympus Optical Co Ltd, Japan) and the distal end of a Trucut biopsy needle. The jaws of the forceps were removed, and the notched central needle of the Trucut soldered to its central wire. The outer cutting sleeve of the Trucut was then soldered to the flexible outer sheath of the forceps.

Photograph of the catheter and adjustable biopsy needle (inset: Cutting end of needle).

The biopsy mechanism relies on the precise axial orientation of the central needle and the sleeve. This was achieved by locating a pin on the needle within a groove cut in the outer sheath. This created a modified Vim-Silverman cutting end attached to a fully flexible shaft of 50 cm with a proximal operating mechanism (figure). It may be sterilised in an autoclave.

As described,^{1,3} the right (or less often the left) internal jugular vein is entered percutaneously using the Seldinger technique, and a 45-cm 9F catheter passed under fluoroscopic control until wedged in a branch of a hepatic vein. The flexible needle is easily passed inside the catheter, and the biopsy specimen taken by advancing the central needle into the hepatic parenchyma and closing the sharp sleeve over it to cut off the specimen. The needle and specimen are removed while leaving the catheter in place, so that further biopsy specimens may be readily taken. Hepatic venography and wedged pressure measurements may also be conveniently performed.

The procedure has been performed by the transjugular approach in 30 patients, most of whom have had prolonged prothrombin times or low platelet counts, and 13 have had cirrhosis. Biopsy specimens were obtained in all 30 patients, and have been diagnostic in all but one. The specimens were of the same size as those obtained by the conventional percutaneous route using a Trucut needle (viz 15-20 × 2 mm), and in particular have shown well the disturbance of architecture in those patients with cirrhosis. They have been greatly superior to specimens previously obtained by the transjugular route.³

Comment

The new needle overcomes the main drawback of the method previously described—namely, the small size and fragmentation of the specimens—while retaining the advantages of the transvenous approach.³ Furthermore, multiple biopsy specimens may be taken without discomfort to the patient once the catheter has been introduced into an hepatic vein, and this may be aimed at a particular site under fluoroscopic control if a localised lesion is suspected. Multiple biopsy specimens may be important in reducing sampling errors—for instance, in assessing chronic hepatitis or cirrhosis—and are useful for additional histochemical or microbiological studies on liver tissue. Also, because of its greater flexibility, this needle will pass into the liver through a catheter introduced through the femoral vein. This approach is being evaluated.

Thus in our experience this design of transvenous liver biopsy needle provides superior specimens and is much easier to use than the rigid needle. As a result, the technique of transvenous liver biopsy may become more widely used when a percutaneous needle biopsy is contraindicated.

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¹ Rösch, J, *et al*, *New England Journal of Medicine*, 1973, **289**, 227.

² Rake, H O, *et al*, *Lancet*, 1969, **2**, 1283.

³ Gilmore, I T, Bradley, R D, and Thompson, R P H, *British Medical Journal*, 1977, **2**, 100.

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Immunisation of adults against diphtheria

In children adsorbed diphtheria vaccine is a safe, effective prophylactic, but in adults, immunisation is complicated by the frequency of severe local and general reactions. Nevertheless, Edsall *et al*¹ immunised young adult Americans with small doses of adsorbed diphtheria toxoid (1 Lf), without Schick testing, and achieved good results with minimal reactions. An adsorbed vaccine containing a reduced amount of diphtheria toxoid (1.5 Lf) and a normal quantity of tetanus toxoid (7.5 Lf) in a single dose was available from Eli Lilly and Company