

Acquired Immune Deficiency Syndrome (AIDS) Manifesting as Anogenital Herpes zoster Eruption: Demonstration of Virus-like Particles in Lymphocytes

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A case of AIDS manifesting as a necrotic, haemorrhagic anogenital herpes zoster and lymphadenopathy, is described. Investigations of T-lymphocyte subsets showed decreased T₄ and slight increase of T₈. Electronmicroscopy revealed tubuloreticular virus-like structures in lymphocytes. *Key words: AIDS; Herpes zoster; Electronmicroscopy; Virus-like structures.* (Received June 5, 1983.)

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Acquired immune deficiency syndrome (AIDS) has been described with increasing frequency among homosexual, young men (1, 2). On the basis of a cellular immune deficiency the mortality rate is very high, and the clinical picture is frequently complicated by various opportunistic infections. Many patients have a prodromal stage of half a year or more characterized by fever, weight loss, lymphadenopathy, lymphopenia and diarrhoea. This report describes a case manifesting as an anogenital herpes zoster eruption. Electronmicroscopically, virus-like particles were demonstrated in lymphocytes from an inguinal lymph node.

CASE REPORT

A 27-year-old bisexual man was admitted to the clinic because of an acute eruption in the anogenital skin area for about 1 week. The patient had been employed as a social worker among drug abusers but had never abused drugs or amyl nitrite himself. 1 ½ years before admission to the hospital he had multiple contacts in homosexual circles in the United States and he had also visited several countries in the Middle East, USSR and America. For about 1 ½ year he complained of weakness and weight loss. During the last year he had recurrent fever and influenza-like symptoms and was confined to bed for periods.

The patient had swollen inguinal and axillar lymph nodes. His eruption was confined to the rima internates and measured about 10×20 cm with haemorrhagic vesicles and bullae, diffuse erythema and some necrotic areas.

Laboratory investigations. Serological tests for syphilis and urethral examinations for gonococci and chlamydia were negative. BSR, Hgb, platelet counts, liver function tests, creatinine, normo-test, quantitation of seroproteins, and X-ray of lungs were all normal. Serological antibody tests against different vira showed: CMV 128 (increased), RSV 8, Coxsackie 8, varicella/zoster 32, HbsAg and anti-HBs were negative. Varicella/zoster virus was grown from the anogenital eruption. Benzidine in faeces was negative. Comprehensive HLA-typing showed the presence of HLA, -A3, -W19, -C40, -CW3, -W4 and -DRW7, while -DR5 was absent. An inguinal lymph node was removed for histological examination. On light microscopy only reactive changes were observed while electronmicroscopic examination revealed the presence of tubuloreticular structures in cisterns of the endoplasmic reticulum of a large number of lymphocytes, and occasionally also in endothelial cells (Fig. 1).



Fig. 1. Lymphocyte. Tubuloreticular structures (T) in endoplasmic reticulum. Note dilatation of tubule with electron dense material (arrow). Nucleus (N). Perinuclear space (S). $\times 102\,000$.

These structures consisted of tubules of undetermined length, with a diameter of about 20 nm. The tubules showed rounded dilatations with a diameter of about 40 nm, spaced 100 nm or more apart. The dilatations contained electron dense material separated from the outer membrane of the tubuloreticular structures by a narrow zone.

Other virus-like structures were not identified, either in the nucleus or the cytoplasm.

Viral cultures including adenoviruses from the urine, were negative.

Immunological investigations. Complete blood counts, including differential white-count showed normal levels of cells, but with a relative lymphopenia. Quantitative determination of serum IgG, IgA and IgM were performed on a Behringwerke Laser Nephelometer. These results showed a hypergammaglobulinemia affecting IgG. C₃ and C-reactive protein were both increased as acute-phase reactants.

The mononuclear-cell population of heparinized venous blood was separated by centrifugation through Lymphoprep (Nyegaard, Oslo). The mononuclear cells were evaluated for surface markers. Immunoglobulin-producing cells (B-lymphocytes) were determined by direct immunofluorescence with FITC-conjugated rabbit anti-human Ig (Makopatts, Copenhagen). The level was within normal limits.

The total T-cell population was estimated using the E-rosette assay, mononuclear cells incubated with sheep red cells treated with (2-amino-ethylisothiuronium bromide hydrobromide (Sigma, St. Louis). The total T-cell level was reduced to 41% (normal 65–85%). The proportion of cells expressing the T-cell antigens T₄ (helper) or T₈ (suppressor) were enumerated using OKT monoclonal

antisera (Ortho Diagnostic Systems, Raritan). The results showed slightly reduced level of T_4 and slight increase in T_8 with a T_4/T_8 ratio of 1.4 (mean normal 2.2).

Lymphocyte-transformation responses were quantitated by a micromethod using the mitogen phytohemagglutinin, concanavalin A and pokeweed mitogen and the antigens candida, mumps, toxoplasmosis, amoebae and purified protein derivative (PPD). Mitogen stimulation compared to normal was impaired. Antigenic stimulation of blastogenesis revealed uniformly depressed incorporation of (3 H) thymidine.

Intracutaneous tests for delayed hypersensitivity to recall antigens showed 1+ reactions for varidase and candida antigen while mumps and PPD were negative.

DISCUSSION

In patients with AIDS the T_4 (helper/inducer) subpopulation is usually found decreased or even absent while T_8 (suppressor/cytotoxic) is found either to be normal or increased (3, 4). This redistribution of the T-cell subsets induces a reversal of the T_4/T_8 ratio which is a sensitive and characteristic component of the immunological alteration that occurs in patients with AIDS and in some healthy homosexuals and hemophiliacs (5). Evidence indicates that an increase in the T_8 subpopulation constitutes a distinctive acquired immune augmentation of T-cell subset. This change " T_8A " is to be distinguished from the decrease in T-helper population that is found in the fully developed AIDS, and can probably be used as prognostic marker (6).

This patient had a slight increase in the T_8 subset but at the same time also a slight decrease in T_4 subpopulation. It is highly probable that the impaired cell-mediated immunity was responsible for the outbreak of herpes zoster eruption. One might also speculate if his homosexual activity predisposed to an eruption in that particulate area. Recently, chronic perianal ulcerative herpes simplex lesions were described in 4 male homosexuals (7). The calculated herpes-directed natural-killer activity was severely depressed in all patients and in 2 inclusions compatible with herpes simplex virus or CMV, were demonstrated.

CMV has been incriminated as a likely pathogenic candidate in AIDS because of its ability to produce alterations in the immune system with reversal of the T_4/T_8 ratio (8, 9, 10) and a microbial agent with spread similar to hepatitis B virus through blood or blood products or for instance through intestinal secretions or semen is one hypothesis. But most probably is the increased titer of CMV in our patient the result and not the cause of the immune defect.

The tubuloreticular structures found by us in the cytoplasm of lymphocytes and endothelial cells have also been observed in lymphocytes of patients with AIDS (2). They are morphologically identical to the structures first described by Sinkovics et al. (11) in lymphocytes from a patient with LED, and subsequently shown to be a regular finding in endothelial cells and lymphocytes in renal biopsies from patients with LED, and have also been found in other immune disorders. It has been suggested that these structures may represent cell products accumulated in response to a latent virus infection, but not a complete virus (12).

Recently, Ewing et al. (13) reported the observation of an unusual cytoplasmic body in lymphoid cells of homosexual men with unexplained lymphadenopathy. Such structures were not observed in our material.

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