

A Case Comparison of Acquired Immune Deficiency Syndrome (AIDS) in Homosexual Males with Spindle-endothelial Cell Abnormalities and with Recrudescant Melioidosis*

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Acquired immune deficiency syndrome (AIDS) is clinically characterised by fatal opportunistic infections such as *Pneumocystis carinii*, *Cryptosporidium* and/or malignancies, notably Kaposi's sarcoma or non-Hodgkin's lymphomas. Prodromal conditions include pre-AIDS (AIDS-related complex; ARC) and lymphadenopathy-associated syndrome (LAS). AIDS affects predominantly homosexual males, intravenous drug abusers, patients with haemophilia A, Haitians, and patients who have had blood transfusions.¹⁻⁸ The syndrome is characterised by a progressive wasting illness, fever and other constitutional symptoms, generalised lymphadenopathy, immune deficiency with an inversion of the T-helper/T-suppressor lymphocyte ratio^{2,8} and the development of opportunistic infections. The clinical and immunological spectrum of AIDS has been gradually expanding to include relatively rare infections such as *Actinomycetales*, *Legionella*, *Campylobacter*, *Salmonella*, *Mucor*, *Cryptococcus*, neoplasms and other immunodeficiencies.¹⁻⁸

In this report we identified the first case of AIDS with Kaposi's

SUMMARY The AIDS syndrome includes cases of biopsy-proven Kaposi's sarcoma in persons under 60 years of age, or biopsy- or culture-proven *Pneumocystis carinii* pneumonia, or either of the life-threatening opportunistic infections in young previously healthy persons with no underlying cause of immunodeficiency (Center for Disease Control criteria). Here we described the first case of AIDS with early Kaposi's sarcoma-like lesions in homosexual male drug addict and have compared the clinical and laboratory findings with those of another homosexual male having recrudescant melioidosis due to *Pseudomonas pseudomallei*.

ASIAN PACIFIC J ALLERG IMMUN 1985; 3:200-204.

sarcoma-like lesions, an American homosexual male, who had a T-cell subset ratio abnormality, spindle-shaped cell and endothelial cell change with extravasation of red blood cells in the dermis. The clinical features and immunological findings of this case are compared with those of another, a German homosexual male with melioidosis due to *Pseudomonas pseudomallei* (Table 1).

CASE REPORTS

Case 1

A 32-year-old American homosexual male drug addict visited Ramathibodi Hospital in December

1984. He had a history of intermittent fever, fatigue, weight loss and chronic diarrhoea of three months' duration. Four years earlier he underwent a radical orchiectomy for a testicular tumour. On admission, the patient's temperature was 38.5°C; blood pressure, 130/80 Torr; and pulse, 120 beats per minute. The right testicle was not enlarged; the left was resected. Inguinal and cervical lym-

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Table 1 Comparison of clinical and laboratory findings of American homosexual drug abuser with those of German homosexual male with recrudescing melioidosis.

	American patient	German patient
Age	32	52
Travelling history	California	Lived in Thailand for more than 10 years
Risk factors identified	Heroin addiction Homosexual	Homosexual
Abnormal chest radiograph	Right basilar infiltrate, patchy	Interstitial infiltrate, left lung
Lung biopsy	Not done	Interstitial pneumonitis
Pathogenic organisms	<i>Candida</i> and <i>Cryptosporidium</i> (small bowel aspirates using String tube)	<i>Candida</i> in oral thrush
T-helper/T-suppressor ratio	0.3	0.34
2,4-dinitrochlorobenzene reaction	None	Not done
Isoprinosine administration	Short course	
Skin-lesion biopsy E.M. study	Spindle cells with dilated rough endoplasmic reticula, abundant mitochondria. Endothelial cells with nuclear pockets. Extravasation of RBCs. Tubular inclusion bodies.	
Other tumour	Testicular tumour removed.	None
HBsAg & HBeAg	Positive	Negative
EBV titre	Positive 1/128	Positive 1/80
Other rare or opportunistic infections	CMV	<i>Pseudomonas pseudomallei</i> (Melioidosis Agent)
Outcome	Returned to home country	Died

phadenopathy was also noted. Multiple purplish-violaceous maculopapular lesions were scattered over his trunk. Biopsies were carried out on three Kaposi's sarcoma-like lesions, 2-4 cm in diameter, on the back of his trunk near the scapular area. Routine laboratory findings were normal. Blood, sputum, stool and urine specimens were negative for pathogens. This patient had hepatitis B surface(s) and e hepatitis antigens (HBsAg and HBeAg positivity) suggesting persistent active viral replication. He also had antibody to the Epstein-Barr antigen

at a titre of 1/128, and antibody to the cytomegalovirus (CMV) at a titre of 1/32.

Laboratory abnormalities included lymphopenia of 1,200-1,500/mm.³ He also had a depressed T-helper lymphocyte level, and a reversed T-helper to T-suppressor lymphocyte ratio of 0.3 (as defined by monoclonal antibody analyses, T-helper=11%; T-suppressor=33%). He also failed to exhibit skin reactivity to 2,4-dinitrochlorobenzene. The chest radiograph revealed right basilar infiltrate. Examination of the small bowel aspirates using the

String tube technique yielded *Candida* and *Cryptosporidium*.

Electron microscopic examination of the biopsied specimens obtained from the Kaposi's sarcoma-like lesions revealed several important findings: there were spindle-shaped cells with abundant cytoplasm containing dilated rough endoplasmic reticula, numerous mitochondria and occasional Weibel-Palade bodies. The endothelial cells showed nuclear pockets, each containing a rounded mass of cytoplasmic material. Such pockets have also been observed in a variety of lymphomas and leukaemia.^{8,13-26} Extravascular red blood cells, a helpful microscopic feature suggestive of Kaposi's sarcoma, and tubular inclusion bodies were also seen. These findings have been thought to be viral in nature and have been described in patients with viral infections, AIDS and collagen vascular disorders.^{8,16}

A more detailed epidemiological history indicated that the patient had been exposed to another American patient with AIDS who died a year and a half before the onset of diarrhoea in this patient.

The patient's temperature had defervesced after the second day of treatment with Isoprinosine (1,500 mg/day), an immunomodulator occasionally used in treating patients with AIDS,¹² and the diarrhoea subsided. Intravenous morphine was also administered during this hospitalisation. After 11 days at Ramathibodi, he left for the United States in late December 1984. Of the two serum specimens obtained from this patient that had been sent to the Cornell University College of Medicine for HTLV-III/LAV antibody testing, one specimen proved to be positive.

Case 2

A 52-year-old German homosexual man was admitted to Ramathibodi Hospital because of haematemesis and melena for four days. On examination the patient was anicteric. His pulse was 132

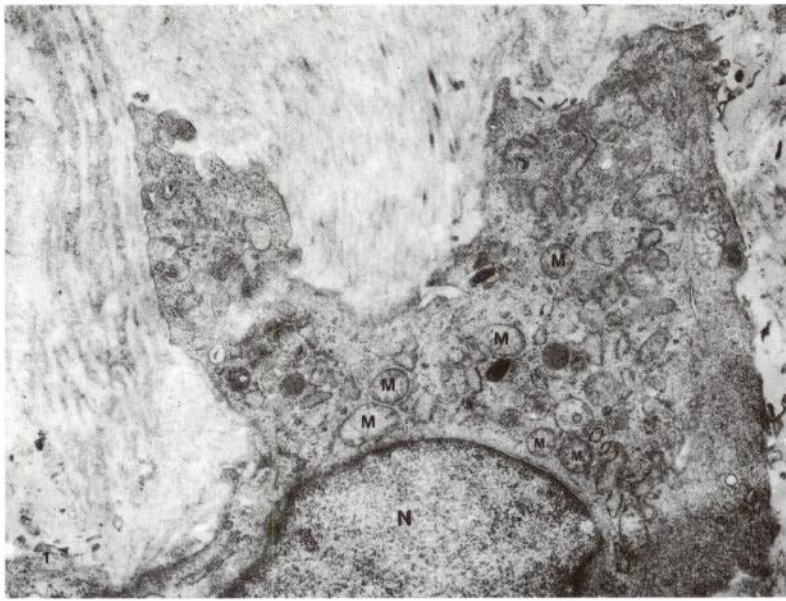


Fig. 1 A portion of spindle-shaped cell with abundant cytoplasm showing moderately dilated cisternae of rough endoplasmic reticulum and numerous mitochondria (M). N = nucleus. (x 18,730)

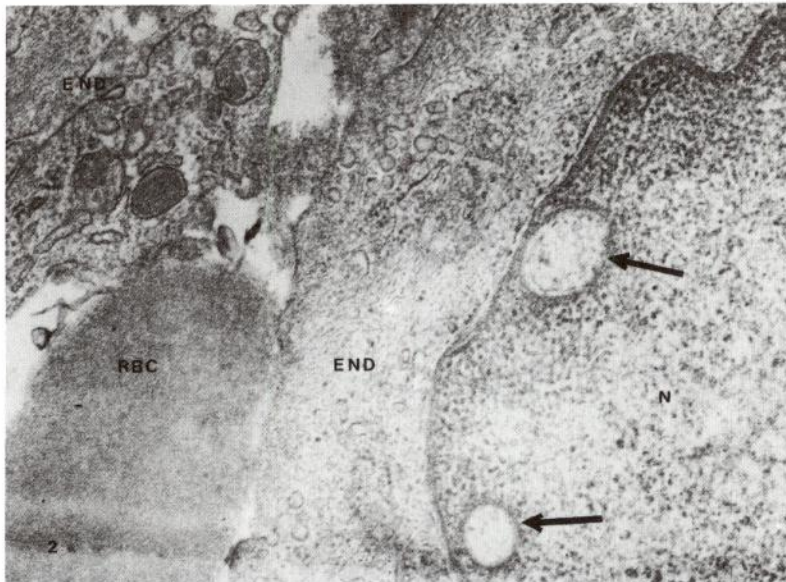


Fig. 2. Endothelial cell with nuclear pockets (arrows). END = endothelial cells; N = nucleus; RBC = red blood cells. (x 52,650)

beats per minute. The edge of the liver descended four finger-breadths below the right costal margin; there were spider naevi and the left flank revealed an old, healed surgical scar. His oral cavity showed thrush, and 1-2 cm nodes were noted over the cervical area. Haematocrit was 20 per cent; the white blood cell count was 3,200,

with 79% neutrophils, 1% band forms, 16% lymphocytes and 4% monocytes. The T-helper/T-suppressor subset ratio was 0.34; total lymphocytes, 512/mm³; and T-helpers, 60/mm³. *Candida* were found on microscopic examination of oral thrush. He also had antibody to the Epstein-Barr virus at a titre of 1/80, and antibody to the cyto-

megalo virus at a titre of 1/16. One serum specimen was positive for HTLV-III/LAV antibody. An exploratory laparotomy was done. During surgery, an oesophago-gastrectomy and anastomosis were performed. Three days later, SGOT was 2,272 International units and SGPT, 895 Ius; bilirubin was 5.4 mg/dl, alkaline phosphatase, 109 units and the LDH, 2,920 units. A chest radiograph showed left upper lobe infiltrates. The patient was given ceftriaxone and metronidazole, but there was no improvement. He died seven days after admission. Post-mortem histological sections of the lung showed interstitial pneumonitis. One of the three blood culture specimens drawn subsequently grew *Pseudomonas pseudomallei*. Past history revealed that several years previously, he had been admitted to a private hospital in Bangkok because of backache; a radiograph of the lumbar spines revealed an inflammatory process at L2-L3. Ten ml of creamy pus drained from the retroperitoneum revealed *Pseudomonas species*. Antitubercular agents had been prescribed and the patient discharged. During 1981-1985 he had been re-admitted on several occasions because of a reaccumulation of pus in the retroperitoneal cavity. Re-culture of the pus revealed *Pseudomonas pseudomallei* with good sensitivity to cotrimoxazole and chloramphenicol. During this time the patient was given cotrimoxazole for melioidosis and then discharged.

DISCUSSION

The primary cause of AIDS is believed to be a lymphocytopathic retrovirus^{9,10} known as lymphadenopathy-associated virus (LAV). Full blown AIDS is the late result of severe T-helper cell immunodeficiency caused after many months or years by retrovirus infection. LAV was first isolated from the nodal tissue of a homosexual male and subsequently recovered from

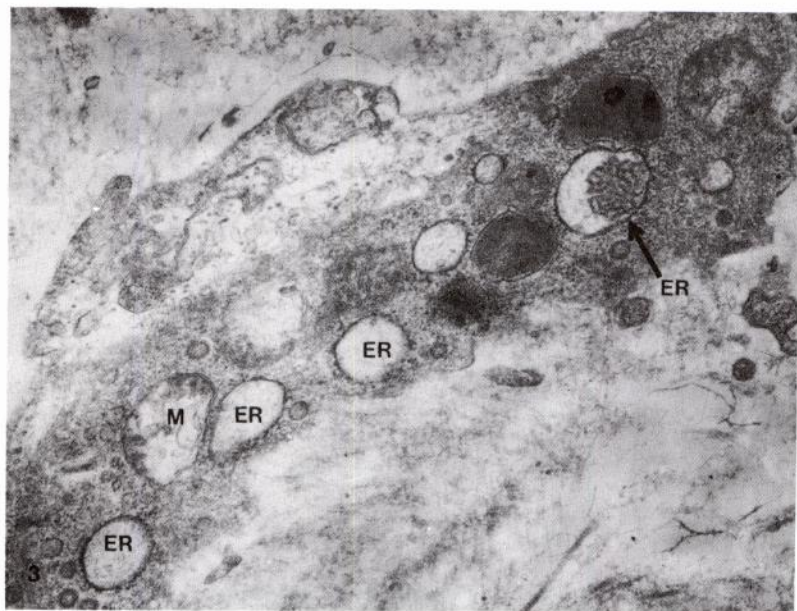


Fig. 3 Tubular inclusion bodies (arrow) within cisterna of rough endoplasmic reticulum (ER). M = mitochondria. (x 29,650)

the T cells of haemophiliacs and other patients with AIDS.^{2,3,6,8,27} The populations that are at high risk for the development of this syndrome are also at high risk of developing hepatitis B virus, CMV and Epstein-Barr virus infections, which all of viruses may play a contributory role in the development of AIDS and Kaposi's sarcoma.^{3,8} Our patient, who was also a HBsAg/HBeAg carrier, had Epstein-Barr virus and CMV infections. Previous studies have shown a reduced ratio of T-helper lymphocyte to T-suppressor lymphocyte in persons with hepatitis B virus-induced chronic active hepatitis. Thirty-five per cent of homosexual men with AIDS have antibody to Epstein-Barr virus.⁸

Recent reports have implicated *Cryptosporidium* and *Isospora belli* species as the cause of diarrhoea and malabsorption in immunocompromised hosts including patients with AIDS. In our American homosexual patient, *Cryptosporidium* species were found in the small bowel aspirates that were obtained by using the String tube technique.^{11,27}

Patients with AIDS often deve-

lop opportunistic infections related to deficient cellular immunity and uncommon malignancies. Although Kaposi's sarcoma is the common tumour diagnosed, undifferentiated non-Hodgkin's lymphoma, plasma cell tumour, cloacogenic carcinoma of the rectum, squamous cell carcinoma of the anus and tongue also occur with greater than expected frequency.⁸ It would be of interest to determine whether such spindle-endothelial cell changes, with extravascular red blood cells suggestive of Kaposi's sarcoma, are seen in other patients with AIDS or ARC.

Opportunistic infections are the principal cause of morbidity and mortality in patients with AIDS. Patients with defective T-cell functions are known to be more susceptible to infections with *Pseudomonas pseudomallei* and intracellular bacteria.²⁸⁻³⁰ Although *Pseudomonas pseudomallei* could be transmitted sexually, there have been no detailed reports of this infection in patients with AIDS. At Ramathibodi, 19 patients over 15 years of age had disseminated melioidosis between 1976 and 1984; however, none of the 19 was homosexual.²⁸⁻³⁰ Patients with dissemi-

nated melioidosis were tested for cell-mediated immunity and many exhibited a cell-mediated defect.²⁸⁻³⁰ Because *Pseudomonas pseudomallei* infections have been associated clinically with defects of cell-mediated immunity, the occurrence of *Pseudomonas pseudomallei* bacteraemia in patients with AIDS was not surprising. The German homosexual male also had concomitant opportunistic infections including *Candida*, Epstein-barr virus and CMV infections, raising the possibility of increased susceptibility to *Pseudomonas pseudomallei*.

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