A Report of Three Cases of AIDS in Thailand*

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SUMMARY Acquired immune deficiency syndrome (AIDS) has been rarely reported as occurring primarily in Asia. We report here on first three cases of AIDS diagnosed at Chulalongkorn Hospital Medical School. One case was an American who had been in Thailand for two years; the other two were Thai. The American and one of the Thai patients were male homosexuals but they had no connection with one another. The latter Thai male homosexual had sexual contact with a German man who showed no evidence of the disease . The other Thai patients was the mistress of the male Thai patient, which underlies the importance of heterosexual transmission of the disease. The two male patients had opportunistic infections whereas the female patient had only generalised lymphadenopathy (Pre-AIDS). Delayed type hypersensitivity response, T-cell subsets enumeration and the *in vitro* T-cell mitogen response served as diagnostic tools when combined with the clinical history. The diagnosis was made even before the results of tests to determine the presence of antibodies to HTLV-III were known. The presence of anti-HTLV-III simply confirmed our diagnosis.

ASIAN PACIFIC J ALLERG IMMUN 1985; 3:195-199

Since its first description in 1981, the incidence of acquired immune deficiency syndrome (AIDS) has increased steadily in the United States[1] and in Europe.[2] Although the disease has been found in patients of Asian origin,[2] case reports from Asia have been scanty. However, with the kind of sexual situation in Thailand, which attracts heterosexual, bisexual and homosexual tourists, it would not be unrealistic to forecast the emergence soon of AIDS in Thailand.[3] We wish to report here three cases of AIDS and AIDS-related complex (ARC) first documented at Chulalongkorn Hospital Medical School during the period February-March 1985.

CASE REPORTS

Case 1

A 30-year-old white American male was first referred to the Immunology Service of Chulalongkorn Hospital Medical School by a private dermatologist in November 1984 for evaluation of his immune status after a five-month history of repeated superficial fungal skin infections. The patient was a homosexual who had lived in the New York area for 10 years before coming to Thailand two years ago with his Black-American male partner. On examination, besides the characteristic monilial infection of the skin over his facial and truncal areas, he also had multiple ulcerated papules with crust formation over his face, trunk, extremities and pinna. *Candida albicans* was cultured from an eczematous skin lesion; *Staphylococcus aureus,* from on ulcer. A biopsy of one of the ulcerated lesions revealed subacute inflammation without neoplastic cells or specific organisms on special stains. He was anergic to all of the six delayed type hypersensitivity (DTH) skin test antigens consisting of PPD, streptolysin, *Candida,* tetanus toxoid, trichyphyton and mumps. His total T cell (E-rosette forming cell) count was 65 per cent (normal 68 ± 6%), OKT-4$^+$ cell, 51 per cent (normal 50 ± 6%), OKT-8$^+$ cell, 40 per cent (normal 30 ± 4%); and the OKT4/T8 ratio, 1.28 (normal 1.6 ± 0.3). Similar results of T-cell subsets were obtained when the tests were repeated two weeks later. In addition, the patient's T cells responded poorly to phytohaemagglutinin stimulation *in vitro.*

The patient was treated with good response using a two-week course of oral cloxacillin and a four-week course of oral and topi-

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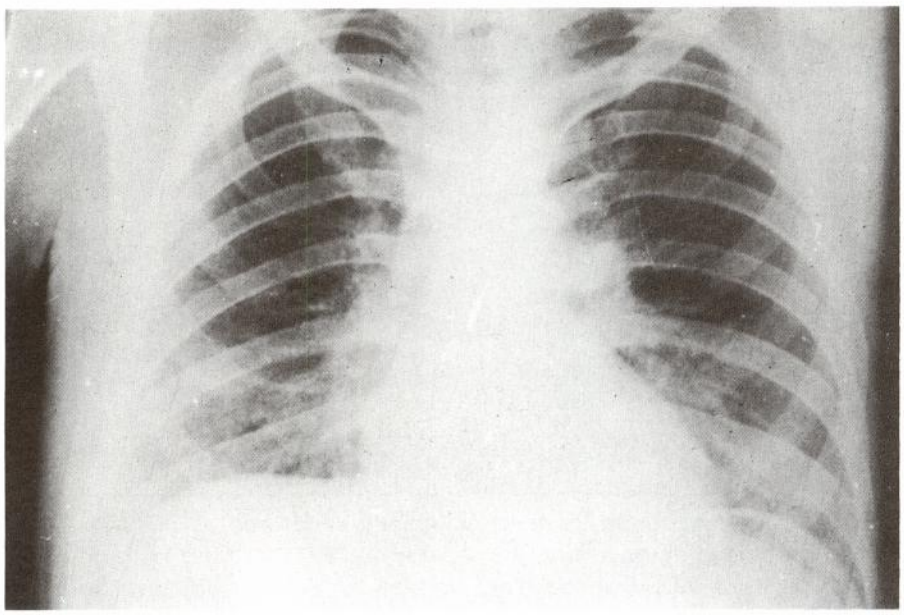

Fig. 1 Chest radiograph of patient No. 1 showing interstitial infiltration in both lower lung fields.

cal ketoconazole for his cutaneous staphylococcal and monilial infections respectively. Three months later (February 1985) he presented a 10-day history of progressive dyspnoea and dry cough. A respiratory rate of 60/min, temperature of 38.0°C and fine bibasilar rales were noted on physical examination. A chest X-ray revealed interstitial infiltration of both lower lung fields (Fig. 1). The patient was then admitted to Chulalongkorn Hospital. CBC, urinalysis, arterial blood gases and blood chemistry were all within normal limits. A pulmonary function study revealed mild restrictive and obstructive lung. A transbronchial lung biopsy revealed numerous *Pneumocystis carinii* on Giemsa stain of a touch preparation (Fig. 2). Haematoxylin and eosin staining of the biopsied lung tissue showed foamy exudate and thickening of the alveolar septa. *Pneumocystis carinii* were also seen in the section after applying Gomori's methenamine silver stain.

T-cell studies during this admission revealed a normal total T-cell count (71%), marked reduction of OKT-4$^+$ cells (20%) and elevation of OKT-8$^+$ cells (46%) with an OKT-4$^+$/T-8$^+$ ratio of 0.4. Impaired T-cell response was still noted both by DTH skin test and by *in vitro* mitogen stimulation. His response to dinitrochlorobenzene sensitisation, however, was intact. Antibody to HTLV-III was positive as performed at the Center for Disease Control Laboratory in Atlanta, Georgia.

One day after hospitalisation, the patient developed oral moniliasis and dysphagia. Barium swallow revealed a coarsening of the lower esophageal mucosa compatible with clinical diagnosis of *Candida esophagitis*. Antibody to *Toxoplasma gondii* was positive (1:4,096). A CT scan of the brain showed parasagital calcification of the vertex. The patient was treated with parenteral co-trimoxasole (15 mg/kg/day of trimethoprim and 75 mg/kg/day of sulfamethoxasole) and oral mycostatin. Temperature returned to normal within three days with marked reduction in cough and dyspnea and disappearance of oral thrush. After 14 days in Chulalongkorn Hospital, the patient was transferred to the USA for extended care.

Added Note: This patient's regular sexual partner (a recipient of anal coitus) for the last 7 years was a 46-year-old black American who also became ill in July of 1985 with *Pneumocystis carinii* pneumonia while still in Thailand. His T-cell subsets and antibody to HTLV-III performed in our laboratory con-

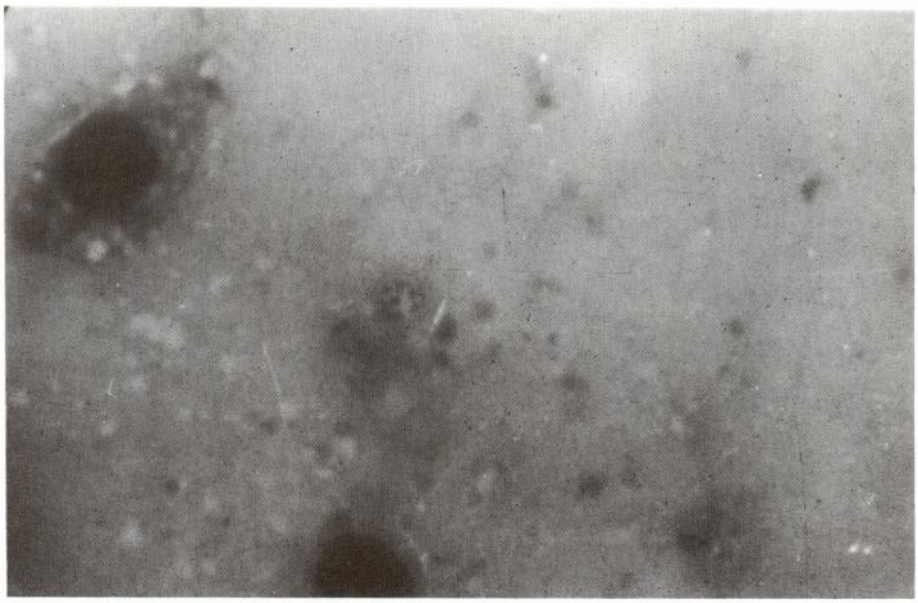

Fig. 2 A touch preparation of the transbronchial lung biopsy specimen of patient No. 1 showing the characteristic eight oval body cyst. (Giemsa's stain ×100).

firmed the diagnosis of AIDS. Following initial stabilisation in Thailand he was referred to the USA.

Case 2

A 27-year-old Thai male first presented to a general hospital on January 16, 1985, having a one-week history of fever, cough and anorexia. Striking bilateral cervical lymphadenopathy was noted and a provisional diagnosis of recurrent tuberculous lymphadenitis was made in spite of a normal chest roentgenogram. The patient was then started on a combined regimen of streptomycin, isoniazid, ethambutol and rifampicin. However, with regard to the fever and lymphadenopathy, no improvement was seen after four weeks of treatment, thus a lymph node biopsy was performed. Pathologic sections revealed caseous granuloma with numerous encapsulated yeasts of varying size suggestive of cryptococcal lymphadenitis. The patient was then referred to Chulalongkorn Hospital Medical School on February 22, 1985 for further investigation and treatment.

This patient's history of cervical lymphadenopathy dated back to May 1982 when he also had fever and a minimal infiltration on chest X-ray. A lymph node biopsy was performed at that time; it revealed caseous granuloma with positive acid-fast bacilli (AFB) staining. A similar regimen of antituberculous drugs was given for a nine-month period with complete resolution of lymphadenopathy and lung lesion. The patient had another episode of fever and cervical lymphadenopathy in July 1983, four months after stopping the anti-tuberculous drugs and was thought to have had infectious mononucleosis without any serologic confirmations. All symptoms subsided spontaneously after 10 days.

The patient was a bisexual for the last 4-5 years. The only male homosexual with whom he ever had contact was a 50-year-old German who visited Thailand every 2-3 months. This German male was completely asymptomatic, had a normal number of T-cell subsets, normal T-cell functions and no antibodies to HTLV-III.

Haemoculture from Case 2 grew *Cryptococcus neoformans.* Examination of cerebrospinal fluid revealed no pleocytosis but encapsulated yeast cells were seen on India ink preparation. However, CSF culture was negative. *Candida albicans* was also recovered from his stool and sputum cultures. Delayed type hypersensitivity skin testing to a battery of skin test antigens was positive only to tetanus toxoid. The response to dinitrochlorobenzene sensitisation was normal.

The percentage of his total T lymphocytes was 68 per cent (normal 68 ± 6%), T4 was 22 per cent (normal 50 ± 6%), T8 was 57 per cent (normal 31 ± 5%) and the T4/T8 ratio was 0.39 (normal 1.6 ± 0.3). The proliferative response of his T cells to phytohaemagglutinin was also significantly suppressed compared to normal controls. Serum was sent to the Center for Disease Control in Altanta, and was found to be positive for anti-HTLV-III.

The patient was started on 150 mg/kg/day of oral 5-fluorocytosine in four divided doses and on amphotericin B in increasing dose up to a daily dose of 20 mg. After 15 days of treatment (total amphotericin B dose of 276 mg), the patient developed a generalised vesiculobullous eruption which was thought to be toxic epidermal necrolysis. Amphotericin B and 5-fluorocytosine were discontinued and a full dose of corticosteroid was given. This resulted in gradual resolution of the skin rash and oral prednisolone was discontinued after 11 days. In addition, because of the uncertainty that *Cryptococcus neoformans* had been completely irradicated with the 15-day course of amphotericin B and 5-fluorocytosine, ketoconazole at a dose of 1,600 mg/day was administered orally soon after the resolution of the skin rash. A total of 46-day course of ketoconasole was given though repeated examinations and cultures for fungus were negative from the blood and CSF. The patient was discharged from the hospital on May 2, 1985 with complete resolution of fever, lymphadenopathy and systemic cryptococcosis although his immunological status remained unchanged.

Case 3

A 26-year-old Thai female was asked to come to the hospital for a complete check-up since she was one of the three mistresses of patient No. 2. She had engaged in regular vaginal intercourse with patient No.2 for the last two years, including a few times during the month prior to patient No. 2's admission to the hospital. She denied having had any anal coitus or having had coitus with any other men.

The patient seemed to be in good health, but generalised lymphadenopathy was noted on physical examination. The size of the lymph nodes, distributed on the bilateral cervical, axillary and inguinal regions, ranged from 2 to 4 centimetres in diameter. She reacted to four out of seven DTH skin test antigens applied. White blood cell count was 12,000/cu mm. with 30 per cent lymphocytes. Seventy-three per cent of the mononuclear cells were T cells (E-rosette forming cells). The percentage of T4 cells was 37 per cent (normal 50 ± 6%) and of T8 cells was 46 per cent (normal 31 ± 5%) with a T4/T8 ratio of 0.8 (normal 1.6 ± 0.3). This ratio dropped further to 0.61 with a further reduction of T4 cells three months later. Anti-HTLV-III was also positive.

COMMENT

Our three cases of AIDS and AIDS-related compelx (ARC) were

diagnosed based on clinical and immunologic data. All of them belonged to the high risk groups for AIDS[1] i.e., the first case was a homosexual, the second case a bisexual and the third case a heterosexual partner of an AIDS case. Both of the male patients had had sexual contacts with homosexuals from countries where AIDS is prevalent, i.e., the United States and West Germany.[2] All were in good health prior to onset of the disease.

The diagnosis of AIDS in case No. 2 was made promptly because of his widespread cryptococcal infection, relative anergy, poor response to *in vitro* mitogen stimulation and characteristic abnormalities of T-cell subsets. Similary, ARC was promptly diagnosed in Case No. 3 by virtue of her clinical history of regular sexual contacts with case No. 2, as well as by the striking generalised lymphadenopathy and the deranged T-cell subsets, although she was not anergic. In contrast, the diagnosis of AIDS was delayed for a few months in case No. 1 who initially had extensive cutaneous candidiasis, anergy and a poor response to phytohaemagglutinin. His T-cell subsets and T4/T8 ratio were marginally abnormal. It was not until *Pneumocystis carinii* pneumonia developed that AIDS could be ascertained since such pneumonia is so characteristic of AIDS.[4-5] In addition, the patient's T-cell subsets also suddenly became abnormal thus supporting this diagnosis.

The diagnosis of AIDS and ARC in our three patients was made before the results of the antibodies to HTLV-III were known. Commercial test kits for anti-HTLV-III became first available in Thailand in early May 1985. Sera from all the patients, including the first serum from case No. 1 were sent to the Atlanta Center for Disease Control; the anti-HTLV-III test results proved positive in all three cases, thus confirming our initial diagnosis. If the anti-HTLV-III test kits had been available to us at the end of 1984, the diagnosis of AIDS in case No. 1 could possibly have been made sooner.

DISCUSSION

Acquired immune deficiency syndrome (AIDS) is an infectious disease that is caused by a new family of retroviruses called human T-cell leukemia virus type III (HTLV-III),[6] which had been described by French researchers as lymphadenopathy-associated virus (LAV).[7] The virus can be isolated from the peripheral blood leukocytes, saliva and semen of some AIDS and ARC patients.[8,9] Antibodies to HTLV-III and LAV can be readily demonstrated in almost all patients and in many asymptomatic individuals at risk of contracting the disease.[10,11]

The virus selectively infects and destroys helper/inducer T cells bearing the OKT-4 and the Leu-3 markers.[12] This results in a relative increase in suppressor T cells, i.e., cells bearing the OKT-8 and the Leu-2 markers, and in the characteristic decrease of the helper/suppressor T-cell ratio.[5,13-15] Suppressor T cells in cases of AIDS with Kaposi's sarcoma were not strikingly increased,[13] in contrast to cases of AIDS with opportunistic infections. Nevertheless, these changes in T-cell subsets serve as one of the diagnostic criteria for AIDS.[5,13]

Increased susceptibility to opportunistic infections and to certain forms of malignancy is thought to be caused by impaired T-helper cells. *Pneumocystis carinii* pneumonia is one of the pathognomic infections encountered in AIDS,[1,4,5] whereas Kaposi's sarcoma is the most common malignancy observed.[1,5]

Diagnostic criteria for AIDS have not yet been clearly defined. The disease is generally diagnosed based on combined clinical and immunological data. Undue susceptibility to opportunistic infections or to Kaposi's sarcoma in a previously healthy individual who belongs to one of the high risk groups for AIDS is the starting point in diagnosing AIDS.[16] Cutaneous anergy with normal or increased serum immuoglobulin levels are commonly found.[5] Lymphopenia, particularly of the T-cell lineage and depressed T-cell response to *in vitro* mitogen stimulation have also been commonly observed.[5,17] Reduction of helper/inducer T cells with or without elevation of suppressor/cytotoxic T cells with the resultant reduction in the helper-to-suppressor ratio together with the presence of antibodies to HTLV-III are generally accepted as the specific diagnostic aids for determining AIDS infection, but these are not without exceptions.[10,11,13-15,18]

ACKNOWLEDGMENTS

The authors wish to thank Dr. Colin Britton and Professor Kachorn Pranich for referring patient No. 1 to our service, and the faculty members and house staff of the Departments of Medicine, Microbiology and Parasitology who helped in the diagnosis and treatment of the patients. We also appreciate the help of Mrs. Wallapa Kaewmora in preparing the manuscript.

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