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Acquired Immune Deficiency Syndrome

— Report of an autopsy case —

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Authors report the first autopsy case of acquired immune deficiency syndrome in Korea. The patient was a 26 years old Korean male who died of respiratory failure due to mixed pulmonary infections. He had history of homosexual contacts with partners of both domestic and foreign nationalities. Initial presentation was unexplained fever for two months. Serological test and western blot test for anti-HIV were positive and T-cell subset analysis revealed T3/T4/T8 to be 73/8/67%. Pulmonary tuberculosis with mediastinal lymphadenopathy and esophagonodal fistula and oral candidiasis were presented. Respiratory infection progressed gradually and he died seven months after the initial symptom. Autopsy findings were generalized severe lymphoid cell depletion, especially of T-cell population and mixed pulmonary infections with Pneumocystis carinii and cytomegalovirus (CMV). The CMV infection involved lungs and adrenals. Oral candidiasis was also demonstrated.

Key Words: *Acquired immune deficiency syndrome (AIDS), Pathology, Pneumocystis carinii pneumonia, Cytomegalovirus.*

INTRODUCTION

Acquired immune deficiency syndrome (AIDS) was first described as a new and distinct clinical entity in 1981 (Gottlieb et al., 1981, Masur et al., 1985). Subsequently, certain other risk groups have been identified in the United States, and a similar disease was emerging at the same time or earlier in parts of central Africa (Perre et al., 1985). Many new cases were reported in many other countries. Numerous epidemiologic, microbiologic, immunologic and pathologic studies have been undergone and finally verified the causative agent to be human immunodeficiency virus (HIV). The pathologic findings and various features of opportunistic infections were also described (Popovic et al., 1984, Gallo et al., 1984, Schuepbach et al., 1984). In Korea, patients who were seropositive for anti-HIV were one and 3 in number in 1985 and 1986, respectively. The number of the seropositive has increased up to 47 by June, 1989. Of them, four patients were diagnosed as AIDS. One case of a young male with Kaposi's sarcoma was presented by Lee et al., in 1988. Authors report an autopsy of a man with AIDS.

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CASE REPORT

Clinical summary

A 27 years old male admitted to the Department of Internal Medicine, Seoul National University Hospital due to fever, dyspnea and non-productive cough in Feb, 1988. He had a previous admission 5 months ago due to fever, cough, odynophagia and weight loss of 7 months duration. At that time the fever was con-

tinuous with minor fluctuation between 38.5-39°C and lasted for 2 months. He was a peddler and lived in Incheon. He had a history of homosexual contacts via rectal or orogenital routes. The sexual partners were multiple, either Koreans or Americans. He was not a habitual intravenous drug abuser and had no blood transfusion. Diagnostic work-ups for the febrile illness revealed pulmonary tuberculosis *(M. tuberculosis)* by sputum smear and culture, multiple hilar and mediastinal lymphadenopathy, esophagonodal fistula on chest CT and endoscopy, and oral candidiasis. He was suspected to have AIDS because of longstanding unexplained fever resistant to antimicrobial therapy. Serological test (ELISA) and western blot test for anti-HIV were positive and T-cell subset analysis was T3/T4/T8; 73/8/67%. Cryptosporidiosis was suspected because of intractable diarrhea, but never confirmed. He was placed on antituberculous medication and the fever subsided.

Thereafter he became relatively well and gained weight for three or four months, when non-productive cough and mild dyspnea developed. He was managed with antitussive agent for 3 weeks. But the above symptoms progressed and fever of 39°C developed. The fever could be controlled with antibiotics and antypyretics and mild fever ranging from 37 to 38°C persisted. Coughing became aggravated.

In the last part of his illness, he complained fatigue, fever and chill, dyspnea and chest tightness. On physical examination, he was very emaciated and chronicaliy ill-looking, and looked dull. Fine crackles were heard in the right lung and left upper lung fields. Diffuse tenderness was noted on abdominal wall and bowel sound decreased. Fingers and toes were cyanotic. Blood pressure was 110/70mmHg, heart rate was 120/min, respiration rate was 30-45/min, and body temperature fluctuated up to 38.5°C. Roentgenogram revealed diffusely scattered nodular densities in both lung fields.

Laboratory findings were as follows; hemoglobin 13.4 gm/dl, WBC count 9000/mm^3 (band/seg/lym; 4/81/11%), platelet count 280K/mm3, ESR 93 mm/h, BUN/Cr 24/0.9 mg/dl, serum protein and albumin 6.3 and 2.7 gm/dl, total bilirubin 0.5 mg/dl, alkaline phosphatase 58 IU/ml, SGOT/SGPT 22/7 IU/ml, Na 142 mEq/L, K 4.0 mEq/L, Cl 107 mEq/L, T-cell subset T3/T4/T8 63/2/68%.

He was treated with trimethoprim/sulfamethoxazole as well as antituberculous medications under the impression of *Pneumocystis carinii* pneumonia and pulmonary tuberculosis. Diarrhea waxed and waned. Infiltrations on chest X-ray films progressed, and he died of respiratory failure after seven months of his illness.

AUTOPSY FINDINGS

Gross examination: The body was that of a emaciated man. The skin lesion was not present. Dorsal surface of tongue was covered by yellowish white granular material, but ulceration was not present. The thymic tissue was not identifiable grossly. Bloody pericardial effusion, about 50 ml, was present. Great vessels and heart were unremarkable. Both lungs showed diffuse consolidation. The right and left lungs weighed 850 and 710 gm, respectively. Cut surface was yellow white. Microcystic spaces were scatterd diffusely and they contained yellow or grayish white mucoid material. Thickening of interstitium was prominent (Fig. 1, 2). Hilar and mediastinal lymph nodes were enlarged up to 1.5 cm. A diverticulum-like pouch was present in the posterior wall of mid-esophagus which probably represented healed fistula tract. Mild fibrosis was noted around the pouch. Peritoneal cavity was clean. The liver, spleen and kidneys were unremarkable. Each adrenal weighed 4.5 gm and

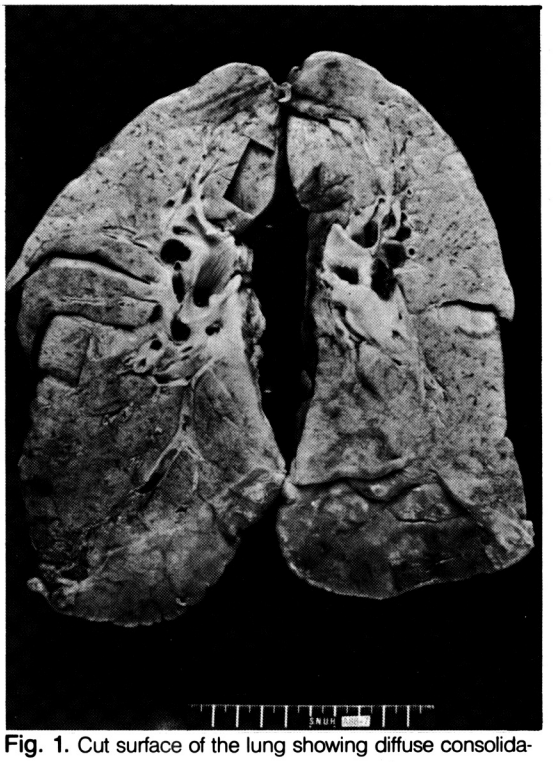

Fig. 1. Cut surface of the lung showing diffuse consolidation. These lungs weighed 1560 gm together.

showed extensive geographic necrosis affecting mainly medulla (Fig. 3). Organizing thrombi were seen in central veins of both adrenal glands. Several ecchymoses measuring 1 to 2.5 cm were scattered in the serosa of the terminal ileum. The brain and meninges were unremarkable. It weighed 1367 gm.

Microscopic examination: In thymus, lymphoid cell depletion was so marked that only epithelial cells and blood vessels were prominent. There were a few scattered calcified Hassall's corpuscles (Fig. 4). Immunohistochemical staining for cytokeratin showed diffuse strong positivity in nearly all epithelial cells which were the major element of cells remaining in the thymus. Lymphocytes stained positive for pan-T marker were scattered but seemed inert and mature. The lymph nodes showed nearly burnt-out appearance. The lymphocyte depletion was also prominent, especially in paracortical area (Fig. 5). A few follicles were remained in cortex but they were disintegrated and showed poorly developed secondary centers in which vasculatures in the follicles were prominent and active follicular center cells were seldom seen. Remaining lymphoid cells seemed to be inert and fully mature. Diffuse plasma cells infiltration was prominent (Fig. 6). Immunohistochemical staining for lymphocyte markers was performed. A few sparsely scattered T cells (Pan-T+) were present in portions. Lymphocytes which looked inert and mature and thought to be B cell were not well-stained with anti-B cell markers (LN-1, LN-2). But staining for kappa and lambda light chains showed diffuse strong positive reactions in these cells.

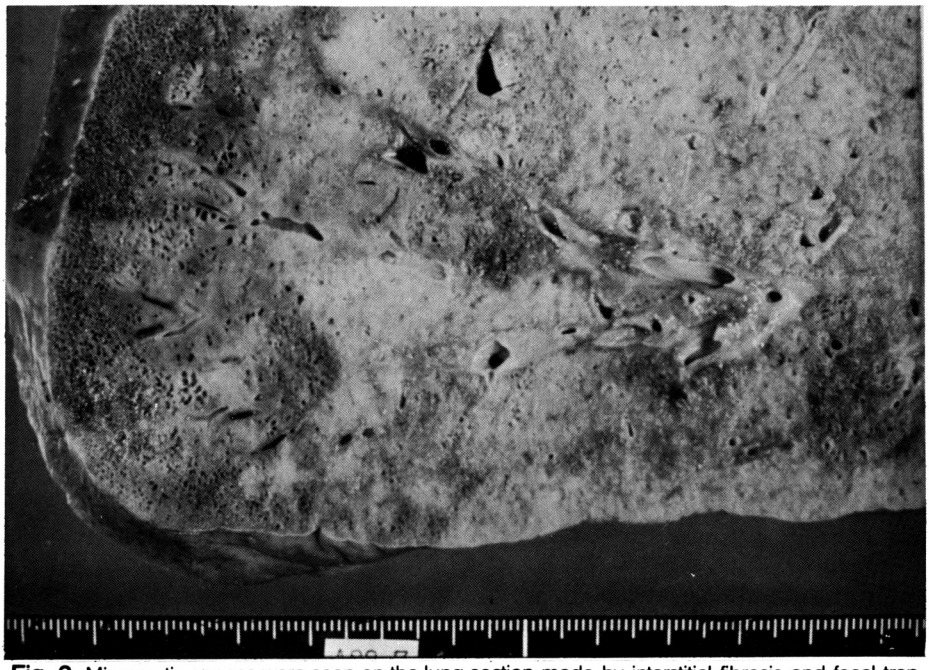

Fig. 2. Microcystic spaces were seen on the lung section, made by interstitial fibrosis and focal trapping of the air.

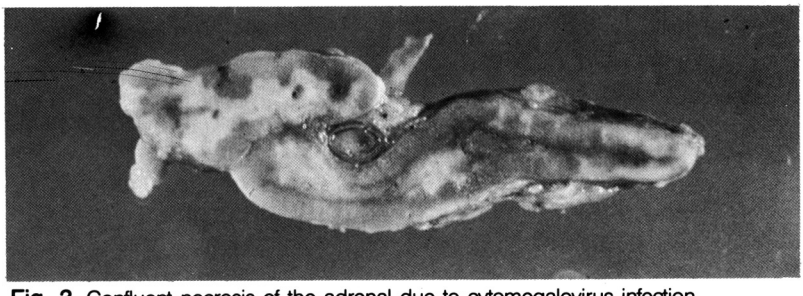

Fig. 3. Confluent necrosis of the adrenal due to cytomegalovirus infection.

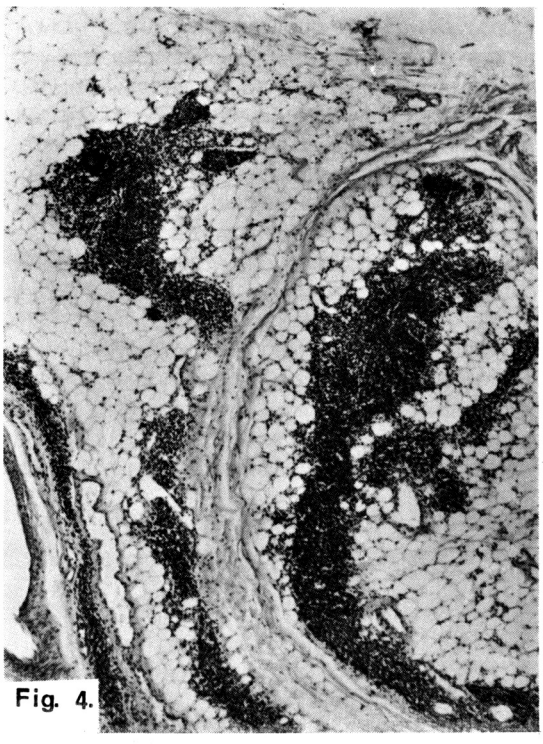

Fig. 4.

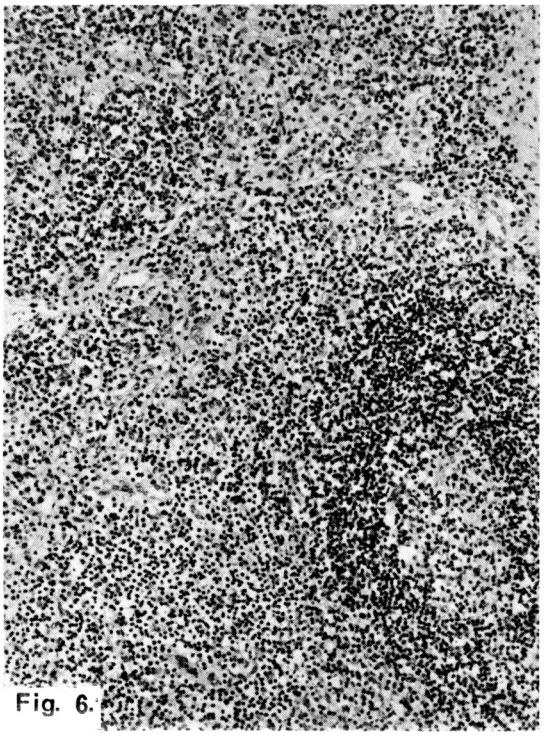

Fig. 6.

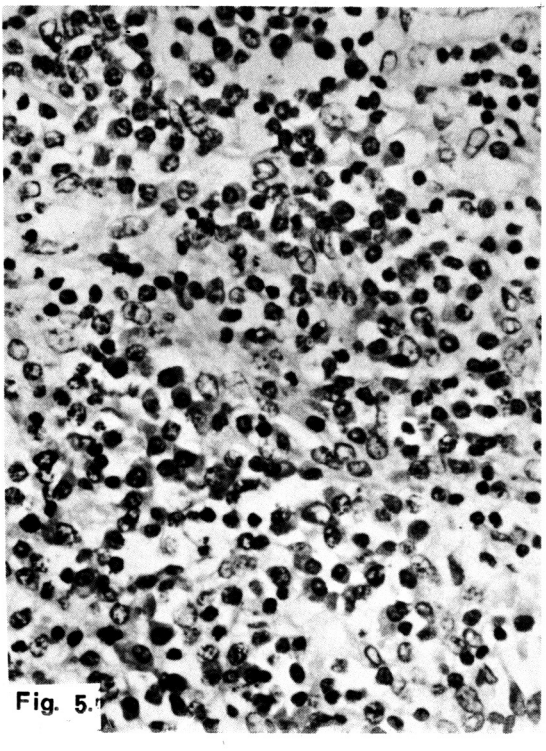

Fig. 5.

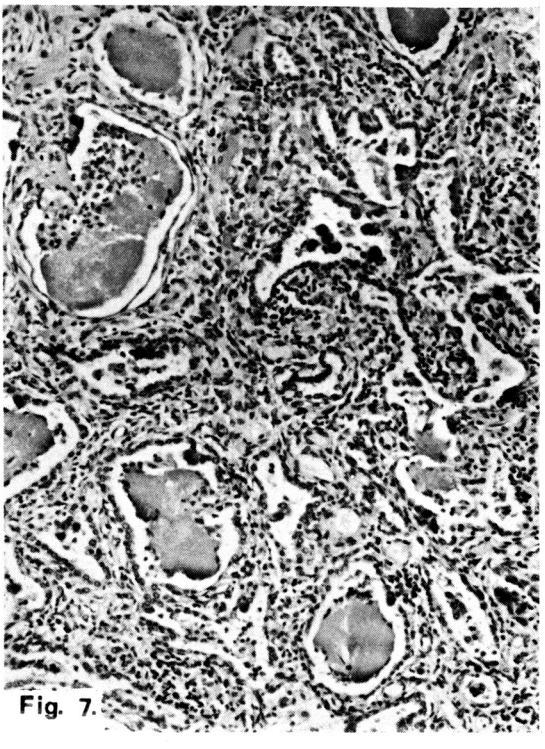

Fig. 7.

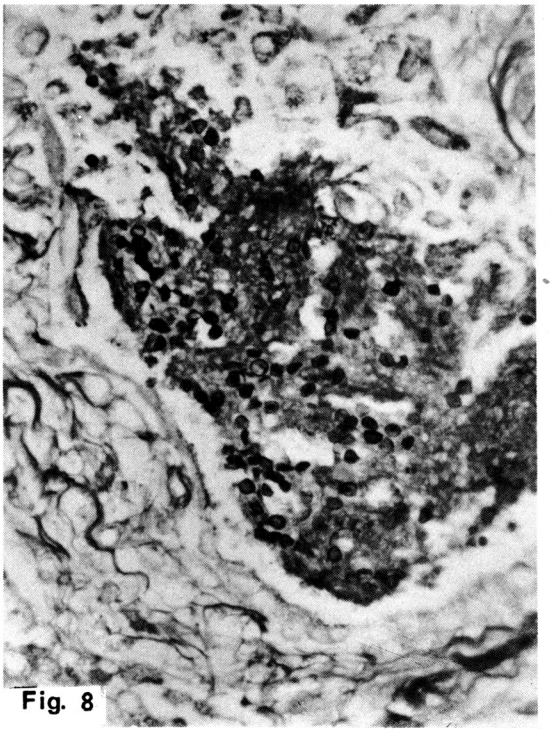

Fig. 8

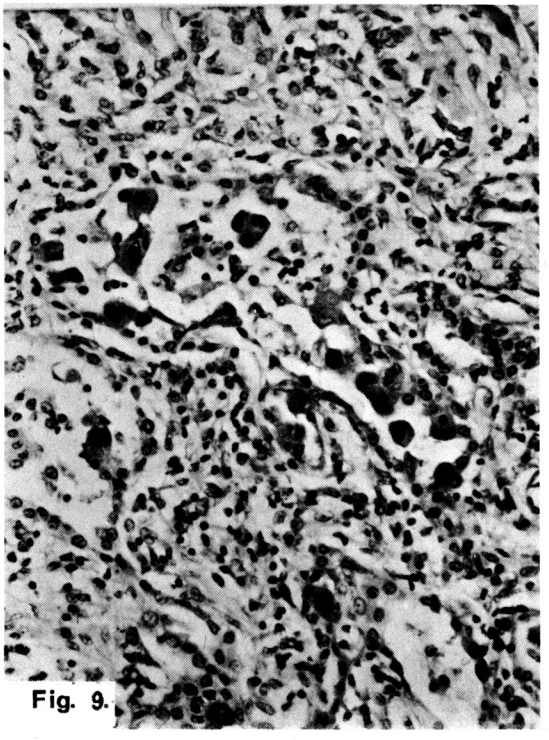

Fig. 9.

Fig. 4. Photomicrograph of the thymus, showing a marked lymphoid depletion and fat replacement. H&E X40.

Fig. 5. Lymph node section showes general depletion of lymphoid cells. A small lymphoid follicle with germinal center is seen in right upper corner. H&E X100.

Fig. 6. High magnification of Fig. 5, showing scattered plasmacytoid cells and depletion of lymphocytes. H&E X400.

Fig. 7. Microscopic picture of the lung, showing interstitial fibrosis, foamy exudate in the remaining alveoli. Focal proliferation of pneumocytes is also seen. H&E X100.

Fig. 8. *Pneumocystis carinii* organisms that are seen as dark navicular structure among exudate. GMS X400.

Fig. 9. Photomicrograph of the lung shows cytomegalic inclusions affecting alveolar lining cells. Note also diffuse small round cell infiltration in the interstitium. H&E X200.

This results represented that the lymphocytes were fully matured. In spleen white pulps were inconspicuous because of severe lymphoid cell depletion. Bone marrow was normocellular, but populations of histiocytes and plasm cells were increased.

In lungs, interstitial spaces were markedly widened by mononuclear cell infiltrations and fibroblastic proliferation. Some alveolar spaces were obliterated and many of the others were filled with foamy or thick eosinophilic exudate (Fig. 7). Among foamy exudate, numerous target-shaped, cup-shaped or crescent cyst forms of *Pneumocystis carinii* were indentified with Gomori methenamine silver stain (Fig. 8). There were many enlarged pneumonocytes containing intranuclear inclusion bodies with prominent peripheral halo (Fig. 9). There were also intracytoplasmic inclusions. The inclusions were characteristic forms of cytomegalovirus (CMV). Among multiple sections there was only a minute focus of epithelioid cell collection. However, acid fast stain failed to demonstrate microorganism in this lesion. Some vessels contained fibrin thrombi. Both adrenals showed severe irregular coagulation necrosis in the cortex and medulla (Fig. 10). The cortex was preserved in portions. In the preserved areas, many scattered cells containing intranuclear and/or intracytoplasmic inclusions were present. There were also fibrin thrombi in some vessels. On the superior surface of the tongue numerous candidal yeasts and mycelia were found, associated with minimal inflammatory cell response. Focal myocarditis and epicarditis were also noted. And a focus of minute mononuclear cell collection was present in cerebral meninges. No other neuropathologic change was present.

Fig. 10. Microscopic picture of the adrenal, revealing focus of coagulation necrosis which is apparently due to cytomegalovirus infection seen in the periphery of the lesion. H&E X40.

DISCUSSION

The acquired immune deficiency syndrome (AIDS) was first recognized in 1981 as a clinical syndrome consisting of opportunistic infection and/or neoplasia associated with unexpected immunodeficiency (Gottlieb et al., 1981, Masur et al., 1985). Subsequently, certain other risk groups have been idenfied in the United States, and a similar disease was emerging at the same time or earlier in parts of central Africa (Perre et al., 1985). Risk groups include homosexual men, intravenous drug abuser, hemophiliacs, especially those treated for their coagulation disorder with factor VIII concentrate, persons with heterosexual contact, etc. Epidemiologic pattern in Korea of the patients infected by HIV is different from in western and African countries in that the prevalence of seropositivity in both general population and the hemophiliacs is low. The number of that patients in homosexual population is also low and the number of the homosexuals is rather low. But this entity become a serious social problem with the increasing number of homosexual population. And increasing number of patients seropositive for anti-HIV call attentions in many respects.

The pathogenesis of the disease begins with alteration and eventual depletion of the T4 cells, which is explained by the fact that HIV has a selective trophism for helper/inducer lymphocytes (Klatzmann et al., 1984, Dalgleish et al., 1984, McDougal et al., 1985) This, in turn, leads to an overwhelming immune dysfunction and eventually to opportunistic infections, CNS diseases, and malignancies. Through autopsy of this case, changes of lymphoid organs were conspicuous; severe lymphoid cell, especially T cell, depletion in thymus, lymph nodes, and spleen. In addition, a feature of moderate plasma cell infiltration in lymph nodes accompanied, which is not a uncommon finding in lymph node of patients with AIDS.

The diagnosis of AIDS is mainly based on the various clinical settings and/or detection of HIV by serological tests. Clinical suspicion in patients with unusual opportunistic infections and unsuspected immune dysfunction is very important. The term AIDS should be reserved for a person with at least one life-threatening opportunistic infection or Kaposi's sarcoma, who has no identifiable reason for profound immunodeficiency. In this sense, this male patient could be diagnosed as AIDS, based on the fact that he had *Pneumocystis carinii* pneumonia, CMV infection of lungs and adrenals, and oral candidiasis, suggesting defect in cell-mediated immunity without specific cause for it.

Patients with AIDS are particularly susceptable to a variety of protozoal, viral, fungal, and bacterial infections. In the patients such opportunistic infections are often severe, persistent, and/or relapsing despite appropriate therapy. Furthermore, numerous simultaneous opportunistic infections frequently occur (Broder, 1987). The frequent opportunistic pathogens are *Pneumocystis carinii,* cytomegalovirus, *Mycobacterium avium intracellulare, and Candida* sp., etc. The *P. carinii* pneumonia is the most frequent pulmonary complication in patient with AIDS. The present case showed pulmonary infection of this organism, which was identified as cyst form best demonstrated with GMS stain. CMV infection is the next most common cause of life-threatening pneumonitis in patients with AIDS. Typically, CMV pneumonia appears late in the clinical course of these patients and signals a poor prognosis. Disseminated infections with CMV may involve a variety of organs in patients with AIDS of which the most commonly involved organs are the adrenal glands, lungs, and gastrointestinal tract (Broder, 1987, Devita et al., 1988) as in this patient. Oral candidiasis was another opportunistic infection. The relapsing diarrhea of this case suggested cryptosporidiosis or CMV infection of gastrointestinal tract. But no organism was found at autopsy. In our case, the patient presented first with pulmonary tuberculosis of *M. tuberculosis* instead of atypical mycobacteria. We thought that the reason for this is the higher prevalence of *M. tuberculosis* rather than atypical mycobacterium in this country. Marked interstitial fibrosis of this patient could not be explained by only mixed pulmonary infection of *P. carinii* and CMV. Oxygenation therapy could have contributed for the fibrosis.

Neurological disease complicates the clinical course in over one-third of patients with AIDS (Broder, 1987, Devita et al., 1988). However, there was no identified lesion in the central nervous system in this case. Kaposi's sarcoma (KS) is the most common tumor associated with homosexual male with AIDS (Broder, 1987, Enzinger and Weiss, 1988, DeVita et al., 1988). In this case, the patient was a bisexual male, but no lesion suggesting KS was present.

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