

# NECROPSY IN HIV-INFECTED PATIENTS

Parnpen Viriyavejakul<sup>1</sup>, Porntip Rojanasunan<sup>2</sup>, Akravudh Viriyavejakul<sup>3</sup>,  
Thanida Tangwanicharoen<sup>1</sup>, Phaiboon Punyarit<sup>4</sup>, Benjane Punpoowong<sup>1</sup>,  
Vasant Khachansaksumet<sup>1</sup>, Panop Wilainam<sup>1</sup>, Emsri Pongponratn<sup>1</sup> and Mario Riganti<sup>1</sup>

<sup>1</sup>Department of Tropical Pathology, Faculty of Tropical Medicine, Mahidol University, Bangkok; <sup>2</sup>Department of Pathology, Faculty of Medicine, Ramathibodi Hospital, Mahidol University, Bangkok; <sup>3</sup>Prasat Neurological Institute, Ministry of Public Health, Bangkok; <sup>4</sup>Department of Pathology, Pramongkutklao College of Medicine, Bangkok 10400, Thailand

**Abstract.** Human immunodeficiency virus (HIV) infection is usually followed by opportunistic infections, especially in the full-blown acquired immunodeficiency syndrome (AIDS). This study details the histopathological changes of different organs in relation to HIV infection, with particular emphasis on the opportunistic infections. Various organs from seventeen HIV-infected patients were collected by necropsy and analyzed for histopathological changes. The major histopathological changes included cytomegalovirus infection, cryptococcosis, penicilliosis, bacterial pneumonia, cryptosporidiosis, pneumocystosis, candidiasis, tuberculosis, granulomatosis of unknown etiology, early cirrhosis and chronic active hepatitis. General organ changes from seventeen cases of HIV-infected patients were described and discussed.

## INTRODUCTION

It is important in the era of the human immunodeficiency virus (HIV) to understand the progression of the HIV-related diseases that often accompany the decline in CD4 levels. As the CD4 count decreases, the immune response to infection is hampered, leading to the acquisition of opportunistic infection. Opportunistic infections are often caused by very important pathogens and may result in the death of an immunocompromised host. Clinical aspects are well defined and have been thoroughly studied. Necropsy in acquired immunodeficiency syndrome (AIDS) started in 1983 in the United States of America after finding of *Pneumocystis carinii* infection of the lungs among homosexuals and disseminated Kaposi's sarcoma in patients during 1981 (Lucas, 1993). In England, Davier *et al* (1994) reported the necropsy rate in AIDS to be 28%

in 1990-1991. Infections vary from place to place and from time to time. In 1996, Lyon *et al* studied the opportunistic infections in AIDS in prison inmates and non-incarcerated patients and reported changing patterns of infections in patients with AIDS; cytomegalovirus was the most prevalent infection; infection with *Pneumocystis carinii* had significantly declined. In third world countries, where AIDS and concomitant opportunistic infections tend to increase with time, pathological studies of necropsy specimens are still limited. The only necropsy study in AIDS in Southeast Asia was recently reported by Viriyavejakul *et al* (2000): opportunistic infections were seen in 47% of cases; the same study reported a wide range of opportunistic infections in the liver of 117 patients, with cryptococcosis (21.4%) as the most outstanding infection, followed by tuberculosis (16.2%), cytomegalovirus (5.1%) and penicilliosis (3.4%). This study reports on the histopathological changes of various organs in HIV-infected patients.

---

Correspondence: Parnpen Viriyavejakul, Department of Tropical Pathology, Faculty of Tropical Medicine, Mahidol University, 420/6 Rajvithi Road, Bangkok 10400, Thailand.

Tel: +66 (0) 2246 900-13 ext 1622; Fax: +66 (0) 2248 3183

E-mail: tmpvr@mahidol.ac.th

## MATERIALS AND METHODS

We included HIV antibody-positive pa-

tients who had died at Ramathibodi Hospital, Mahidol University, Bangkok, and Pramongkutkloao Military Hospital, Bangkok. The nearest relative gave written informed consent for organ necropsy having been given on explanation of the objectives of the study and its procedures. Organ necropsy was performed using either a disposable liver biopsy set according to Menghini (biopsy needle size 15 G/1.8 mm, needle length 88 mm, distance sleeve 18 mm, bevel 45°) or a mini-laparotomy technique. Organ tissues were immediately fixed in 10% formalin for 48 hours; processed in series of alcohol, acetone and melted paraffin; embedded in paraffin blocks and sectioned with a microtome to the thickness of 3-4 microns. Slices of tissues were laid on a clean and dry glass slide and stained with modified Hematoxylin and Eosin (H&E) stain for initial pathological evaluation. Pathological changes of the organs were recorded. Detection of organisms was by special staining techniques. The stains included Kinyoun's stain, Taylor's stain, Periodic Acid Schiff's stain (PAS), Gomori Methenamine stain (GMS) and Mucin stain. Masson Trichome stain was used to identify early fibrosis in cases such as chronic active hepatitis. Data were analyzed and presented by descriptive study.

## RESULTS

We were able to conduct organ necropsy for seventeen HIV-infected patients. We included cases that enabled the pathological evaluation of at least two organs. Table 1 summarizes the major histopathological diagnosis of the 17 necropsy cases and the involved organs. There were two cases each of cytomegalovirus infection, (with one co-infected with *Cryptosporidium*), cryptococcosis, penicilliosis (one case associated with early cirrhosis), bacterial pneumonia; one case each of cryptosporidiosis, pneumocystosis, candidiasis, tuberculosis, granulomatosis of unknown etiology and early cirrhosis; there were three cases of chronic active hepatitis. Clinical data were available in only four cases. Two cases

had compatible clinical and pathological diagnoses (cases 2 and 3). Case 11 was clinically diagnosed as merely bacterial peritonitis with no etiologic agent specified. The necropsy specimens however, disclosed miliary tuberculosis involving the major organs. The cause of death of case 13 was unknown: the patient had multiple small papules over the face and body and she died shortly after admission; systemic penicilliosis was discovered from the necropsy specimens. Presence of bacteria in cases 6 and 10 in the large intestine could have been attributable to post-mortem colonization. One case showed unremarkable changes (case 12).

### Heart

Heart tissue was obtained in 10 cases. Pertinent pathological changes included the thickening of blood vessels by collagen deposits, irregularly arranged myocardial fibers, brown atrophy, enlarged nucleus, petechial hemorrhages, thrombus (sterile) formation, focal calcification and endothelial proliferation.

### Lungs

Pathological changes in the lungs were detected in 7 of 11 cases. Cytomegalovirus infection, cryptococcosis, pneumocystosis and tuberculosis were the opportunistic organisms. There was no inflammatory response associated with the above organisms. Tissue changes in tuberculosis varied from presence of spotty necrosis and vague granuloma to well-formed granuloma with and without organisms. A case of bronchopneumonia (bacterial) was noted with bronchial destruction. Adult respiratory distress syndrome was a common finding. It was usually associated with intra-alveolar macrophages, severe congestion and edema and minimal hemorrhage.

### Liver

Generally, the liver seemed to be the most accessible organ for necropsy. The liver architecture was preserved. Pathological changes ranged from normal to severe destruction of hepatocytes due to opportunistic organisms. Cryptococcosis (2), penicilliosis (1) and tuber-

Table 1  
Major histopathological diagnosis of 17 HIV-infected patients and the involved organs.

Cases	Histopathological diagnosis	Organ necropsy	Organs with major histopathology
1	Cytomegalovirus infection, cryptosporidiosis	Heart, lungs, liver, spleen, kidneys, pancreas, adrenal glands, lymph node, stomach, small and large intestines, brain	Small and large intestines (cryptosporidiosis) including vermiform appendix
2	Cryptococcosis	Lungs, liver, spleen, kidneys, pancreas, adrenal glands, stomach, small intestine, muscle, diaphragm, skin	Lungs, liver, spleen, kidneys, pancreas, adrenal glands, skin
3	Cytomegalovirus infection	Heart, lungs, liver, spleen, kidneys, pancreas, stomach, small and large intestines	Lungs, large intestine
4	Bacterial pneumonia	Heart, lungs, liver, spleen, kidneys, pancreas, skin	Lungs
5	Bacterial pneumonia	Heart, lungs, liver, spleen, pancreas, adrenal glands, small and large intestines	Lungs
6	Pneumocystosis, gram-positive diplococci	Heart, lungs, liver, spleen, kidneys, pancreas, adrenal glands, stomach, small and large intestines	Lungs, large intestine (gram positive diplococci)
7	Chronic active hepatitis	Heart, lungs, liver, spleen, kidneys, pancreas, adrenal glands, stomach, large intestine, skin	Liver
8	Granulomatosis	Heart, lungs, liver, spleen, kidneys, pancreas, adrenal glands, stomach, large intestine, brain	Lungs, liver, spleen
9	Candidiasis,	Spleen, lymph node	Spleen, lymph node
10	Chronic active hepatitis, gram positive rods	Heart, lungs, liver, spleen, kidneys, pancreas, adrenal glands, lymph node, stomach, small and large intestines, brain, skin, bone	Liver, large intestine (gram positive rods)
11	Tuberculosis	Heart, lung, liver, spleen, kidneys, pancreas, lymph node, stomach, small intestine, skin	Lungs, liver, spleen, kidneys, lymph node
12	Not remarkable	Heart, lungs, liver, spleen, kidneys, pancreas, adrenal glands, large intestine, skin, uterus, ovary	None
13	Penicilliosis	Liver, skin	Liver, skin
14	Early cirrhosis, fatty steatosis	Liver, skin	Liver
15	Cryptococcosis, adult respiratory distress syndrome	Lung, liver, skin	Lungs (adult respiratory distress syndrome), liver
16	Chronic active hepatitis	Liver, muscle	Liver
17	Penicilliosis, early cirrhosis	Liver, diaphragm	Liver

culosis (1) were the three common infections. There was a very minimal or an absent inflammatory response in the presence of organisms. Granulomatous changes were usually devoid of typical Langhans' giant cells, with or without organisms. Chronic active hepatitis was seen in 3 of the 16 liver samples; early cirrhosis was evident in two. Other changes included mild-moderate-severe fatty steatosis, single cell degeneration, eosinophilic granules within hepatocytes, reactive Kupffer cells, periportal fibrosis, portal inflammation and increased collagen in the portal tracts.

### Spleen

We were able to obtain tissue from the spleen in 12 cases, four of which showed opportunistic infections (33.33%). Severe cryptococcosis, candidiasis, tuberculosis and granulomatous of unknown etiology were seen. There was no inflammatory response in the presence of organisms, only spotty necrosis accompanied tuberculosis. The spleen commonly showed a decrease in white pulps and sclerotic blood vessels and an increase in collagen deposits, histiocytes, and thickening of the capsule. One case showed atypical lymphoid hyperplasia.

### Kidneys

Ten kidney tissue samples were collected. Among the opportunistic infections, only cryptococcosis and tuberculosis were present (one case each). Cryptococcus was seen in the capillary loop, suggestive of disseminated involvement. Changes related to tuberculosis were spotty necrosis, otherwise the inflammatory response was negligible. Other changes were focal segmental glomerulosclerosis, focal calcification, acute tubular necrosis, mesangial proliferation, mesangial thickening, sclerotic blood vessels, chronic interstitial nephritis, congestion and minimal autolysis.

### Pancreas

There was one case of cryptococcosis from 11 preserved tissues obtained (9.09%). It showed no inflammatory response in the presence of

very few organisms. Enlarged islet cells of Langerhans were seen in one case; the cells within the islet cells were generally hypertrophied. Some specimens contained atypical lymphoid cells.

### Adrenal glands

Eight tissues sample from adrenal glands were obtained. Cryptococcosis was detected in one case, which showed no inflammatory response. Other pathological changes included vacuolization and congestion.

### Lymph nodes

Lymph node samples were obtained in two cases: both harbored infectious agents. Generally, lymphoid depletion and sinus histiocytosis were evident. Opportunistic infections included candidiasis and tuberculosis; changes related to tuberculosis were spotty necrosis.

### Small intestine

The specimens were generally well preserved. Cytomegalovirus within the endothelium was detected in one of the seven tissue samples from the small intestine (14.26%). Cryptosporidiosis was present and was attached to the brush borders. Some cases showed bacteria colonization, lymphoid hyperplasia and eosinophilia within the lamina propria.

### Large intestine

Nine tissue samples from the large intestine were included. Cytomegalovirus was seen in the endothelial cells and within the muscular layer of the large intestine: it induced severe necrosis and destruction of intestinal villi as well as smooth muscle cells. Organisms showed different stages of development. Other findings were presence of atypical lymphoid hyperplasia, presence of bacteria on the intestinal mucosa and increased mucosal mitosis.

### Skin

Nine skin tissue samples were collected. Two cases (22.22%) harbored opportunistic infections, *ie* cryptococcosis and penicilliosis.

One case showed gram-positive cocci. Another case showed chronic folliculitis and elongation of the rete ridge.

### Other tissues

We obtained tiny tissue samples from the brain (3 cases) and from muscle (2), diaphragm (2), bone (1) uterus (1) and ovaries (1): all were unremarkable. Tissues from the stomach (8) showed autolysis.

## DISCUSSION

We studied the spectrum of pathological changes associated with HIV-infection in different organs. The changes depended on the response of the patients. As the immune response fails, the chances of opportunistic infection increase. Generally, organ involvement usually represents part of a widely-disseminated disease. Aside from histopathological changes induced by opportunistic infections, the use of antiviral drugs and the duration and effects of HIV infection itself lead to a variety of pathological changes in different organs.

### Heart

We did not find myocarditis as previously reported (Giamplamo *et al*, 1989; Kaul *et al*, 1991). Sterile thrombus formation detected in one case may have been a manifestation of terminal disease process. Changes noted were unique and suggestive for HIV infection but not specific. It was interesting to note a variation of histopathological changes not seen in normal heart tissue.

### Lungs

Opportunistic infections were the major findings in the lungs (63.64%). We found a variety of infectious agents: viruses, bacteria and fungi. The absence of inflammatory responses is secondary to a marked deficiency in the immune response to infection in HIV-infected patients. We did not find interstitial inflammation as often as did earlier research-

ers (Giamplamo *et al*, 1989). Our series happened to include long standing HIV patients whose immune response was no longer active. On the other hand, adult respiratory distress syndrome was common. Moran *et al* (1994) reported *Pneumocystis carinii* pneumonia as being the most prevalent type of infection, followed by bacterial pneumonia.

### Liver

In a series of 117 necropsy liver tissue samples, Viriyavejakul *et al* (2000) found no histologic feature in the liver specific for human immunodeficiency virus infection. Opportunistic infections, however, were prevalent. Malignancy *per se* was absent from the samples; it is more common in western countries where Astagneau *et al* (1990) reported 19% with Kaposi's sarcoma of the liver.

### Spleen

The spleen, as an important immune defense organ displayed changes related to an immunodeficient state. The decrease in white pulp was seen in nearly all cases. As a result, histiocytes predominated in the sinuses. The presence of atypical lymphoid cells could be the early progressive change to malignant lymphoma.

### Kidneys

HIV-associated nephropathy has previously been described (Carbone *et al*, 1989, Giamplamo *et al*, 1989). It is commonly associated with full-blown AIDS and rapidly progresses to uremia. From our study, aside from infectious process, glomerular changes were common: focal segmental glomerulosclerosis and mesangial thickening and proliferation. Segmental necrosis was previously reported (Giamplamo *et al*, 1989), but not seen in our study.

### Pancreas

The incidence of opportunistic infections in the pancreas was low despite the high prevalence of infection in other organs. Even in disseminated cases, the pancreas is quite re-

sistant to infection. However, in pediatric patients with AIDS, Kahn *et al* (1995) reported acute pancreatitis in 17%; acute pancreatitis can also be caused by didanosine therapy (Veny *et al*, 1995).

### Adrenal glands

Cryptococcosis of the adrenal glands in our study was the result of disseminated disease rather than primary organ involvement. This may be related to adrenal insufficiency, which may remain undetected clinically. Giampalmo *et al* (1989) found cytomegalovirus infection to be the most common change in the adrenal glands.

### Lymph nodes

Four histological patterns common in HIV-infected patients are follicular hyperplasia, follicular fragmentation, follicular atrophy and follicular depletion. Most of the AIDS patients showed lymph node changes compatible with follicular atrophy and follicular depletion (89%) (Biberfeld *et al* 1987). The only two lymph nodes obtained were from patients with full-brown AIDS. Aside from follicular lymphoid depletion, we noted sinus histiocytosis as a reactive process in both cases. This may be a secondary response to the infectious process or merely an immune response to HIV infection.

### Small and large intestines

Cytomegalovirus colitis has been reported (Gonzales *et al*, 1987). It is usually the result of severe immunocompromise and is commonly associated with systemic involvement.

### Skin

Cutaneous lesions in Thailand often indicate infectious processes. Malignancy such as Kaposi's sarcoma is rare, unlike the pattern of malignancy in western countries (Astagneau *et al*, 1990).

We did not observe malignancy in our series, although the presence of atypical lymphoid cells in the spleen and pancreas may be

a sign of progressive development to malignant lymphoma. Opportunistic infections seemed to predominate. We can conclude that histopathological changes of various organs are neither unique nor specific for HIV and that necropsy or autopsy is vital for a better understanding of the spectrum of human immunodeficiency virus infection.

### ACKNOWLEDGEMENTS

This study received financial support from Mahidol University, Bangkok, Thailand. We would like to thank to the Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand for generously supporting the publication of this study. The assistance of Mr Wirat Pingwon, Miss Wimol Yomana, Mrs Patcharee Boonachot, Mr Mana Chimsawat and Mrs Namvaew Punpongpaew is gratefully acknowledged.

### REFERENCES

- Astagneau P, Michon C, Marche C, *et al*. Hepatic involvement in AIDS. A retrospective clinical study in 71 patients. *Ann Med Intern* 1990; 141: 459-63.
- Biberfeld P, Ost A, Porwit A, *et al*. Histopathology and immunohistology of HTLV-III/LAV related lymphadenopathy and AIDS. *Acta Pathol Microbiol Immunol Scand A* 1987; 95: 47-65.
- Carbone L, D'Agati V, Cheng GT, Appel GB. Course and prognosis of human immunodeficiency virus-associated nephropathy. *Am J Med* 1989; 87: 389-95.
- Davies J, Everall IP, Lantos PI. Post mortem examination of HIV infected patients. *Curr Opin Infect Dis* 1994; 7: 456-62.
- Giampalmo A, Ardoino S, Borghesi MR, *et al*. Anatomic-pathologic findings in 25 autopsy cases of AIDS. *Pathologica* 1989; 81: 1-46.
- Gonzales Cueto D, Maffei ME, Patito A, Campos MM. Colitis caused by cytomegalovirus in acquired immunodeficiency syndrome. Report of 2 cases of autopsy. *Acta Gastroenterol Latinoam* 1987; 16: 273-8.
- Kahn E, Anderson VM, Greco MA, Magid M. Pancre-

- atic disorders in pediatric acquired immune deficiency syndrome. *Hum Pathol* 1995; 25: 765-70.
- Kaul S, Fishbein MC, Siegel RJ. Cardiac manifestations of acquired immune deficiency syndrome: a 1991 update. *Am Heart J* 1991; 122: 535-44.
- Lucas S. HIV and the necropsy. *J Clin Pathol* 1993; 46: 1071-5.
- Lyon R, Haque AK, Asmuth DM, Woods GL. Changing patterns of infections in patients with AIDS: A study of 279 autopsies of prison inmates and non-incarcerated patients at the University hospital in Eastern Texas, 1984-1993. *Clin Infect Dis* 1996; 23: 241-7.
- Moran CA, Suster S, Pavlova Z, Mullick FG, Koss MN. The spectrum of pathological changes in the lung in children with the acquired immunodeficiency syndrome: an autopsy study of 36 cases. *Hum Pathol* 1994; 25: 877-82.
- Veny A, Romeu J, Raventos A, Lopez MP, Sirera G, Clotet B. Acute pancreatitis in patients infected with human immunodeficiency virus. *Rev Clin Esp* 1995; 195: 614-9.
- Viriyavejakul P, Rojanasunan P, Viriyavejakul A, *et al.* Opportunistic infections in the liver of HIV-infected patients in Thailand: A necropsy study. *Southeast Asian J Trop Med Public Health* 2000; 31: 663-7.