

## HISTOPATHOLOGICAL STUDY ON GRANULOMA FORMATION AGAINST CRYPTOCOCCI IN PATIENT WITH ACQUIRED IMMUNODEFICIENCY SYNDROME WITH AND WITHOUT TREATMENT OF ACTIVE ANTIRETROVIRAL THERAPY

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**Back ground and aim:** The recent acceptance of antiretroviral therapy has had a dramatic impact on the epidemiology and clinical characteristics of many opportunistic infections associated with human immunodeficiency virus. Interactive opportunistic infections are now less common. The present paper describes details of the histopathological features of cryptococcal infection in a patient with acquired immunodeficiency syndrome (AIDS) who had been treated with active antiretroviral therapy, compared with those in patients without combination therapy as well as in immunocompetent patients.

**Design:** eighteen autopsies of AIDS without active antiretroviral therapy, an autopsy of AIDS treated with zidovudine, lamivudine and indinavir in combination, and seven pulmonary lesions of cryptococci developed in immunocompetent patients were employed for the investigation. Sections of each lesion were stained, routinely, and observed both under light microscopy and with confocal laser scanning microscope equipped with argon laser source for morphometric analysis and three dimensional observation on multinucleated giant cells.

**Result:** Massive cryptococcal proliferation was demonstrated and resulted in destruction of pulmonary architecture with hemorrhage in patients with AIDS who were not treated with active antiretroviral therapy. Histiocytic response with a formation of multinucleated giant cells varied in case to case, but not prominent. An essential feature of them was massive capillary involvement with poor response of histiocyte. None were visible of CD4+ cells. On the other hand, the autopsy with a treatment of active antiretroviral therapy revealed generalized cryptococcal infection, but foci in the lung were characterized by scattered defined nodules consisting of proliferating yeasts, numerous histiocytes and multinucleated giant cells of foreign body type. Each nodule was encompassed by thin fibrous tissue, and there were organized thrombi in pulmonary arteries involved by cryptococcal lesions. Immunohistological examination revealed CD4+ cells at periphery of each lesion. There were packed matured multinucleated giant cells with an intervention of CD4+ cells in typical cryptococcal granulomas in immunocompetent individuals.

**Conclusion:** The histological characteristics of cryptococcal infection in patient treated with antiretroviral agents are 1) better formation of multinucleated giant cells and 2) restriction of cryptococcal proliferation in ischemic areas.