ACQUIRED IMMUNODEFICIENCY SYNDROME

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PATHOGENESIS:

HIV is a retrovirus of lentivirus family which causes the acquire immunodeficiency syndrome. HIV infection leads to destruction of the immune system and the infected persons would develop opportunistic infections and neoplastic diseases.

The great majority of AIDS cases are caused by HIV-1. HIV primarily infects cells with CD4 cell surface receptor molecules including cells of the mononuclear phagocytic system (CD4 lymphocytes, blood monocytes, tissue macrophages, dendritic cells and microglial cells).

HIV has the additional ability to mutate very easily and resist to drug therapy.

A second HIV designated HIV-2 is mostly present in West Africa but only sporadically elsewhere. The transmission of HIV-2 is similar to HIV-1, but the perinatal transmission is much less frequent, a less aggressive course of AIDS, and a lower viral load with higher CD4 lymphocytes count. The mortality rate of HIV-2 infection is only two-thirds of HIV-1.

Replication of HIV may first occur within inflammation cells at the site of infection or within peripheral blood mononuclear cells but it quickly shifts to lymphoid tissue of the body. First HIV viruses are trapped in the processes of follicular dendritic cells where they may infect CD4 lymphocytes.

Mothers With HIV infection can pass the virus transplacentally, at the time of delivery through the birth canal or through breast milk.

Congenital AIDS occurs in about 25-30% of babies from HIV-1 infected mothers.

Acute HIV infection may produce a mild disease resembling infectious mononucleosis that diminishes over 1-2 months.

Generally, within 3 weeks to 3 months an immune response is accompanied by a simultaneous decline in HIV viremia and presence of positive serologic HIV tests.

A clinical latent period of HIV infection lasts an average from 8 to 10 years during which time enough of the immune system remains intact to prevent most infections, but viral replication actively continues in the lymphoid tissue, a decrease in the total CD4 count below 500/ul presages the development of clinical AIDS and a drop below 200/ul not only defines AIDS, but also indicates a high probability for the development of AIDS-related a high probability for the development of AIDS-related opportunistic infection and / or neoplasms.

HIV - RELATED LYMPHADENOPATHY:

HIV - related lymphadenopathy can be seen in the absence of opportunistic infections or neoplasms. Follicular hyperplasia, follicular hyperplasia with fragmentation of lymphoid follicles with focal hemorrhage, follicular involuting and follicular depletion with copmlete absence of the lymphoid follicles are

features seen in HIV-related lymphadenopathy.

LYMPHOEPITHELIAL CYSTS ASSOCIATED WITH HIV INFECTION:

The morphologic changes in this condition includes lymphoepithelial cysts similar to those seen in solid lymphoepithelial lesions with epimyoepithelial islands or the lesion seen in Mikulicz's disease or a combination of both. The cysts are lined by squamous or glandular epithelium surrounded by a florid lymphoid hyperplasia with prominent germinal centers. The lymphoid follicles show prominent network of HIV-infected dendritic reticular cells and numerous interfollicular CD8 lymphocytes.

LYMPHOID INTERSTITIAL PNEUMONITIS:

LIP is a diagnostic criterion for AIDS patients in childhood but is not frequently seen in adults. The tissue diagnosis is made by open lung biopsy. Peripheral blood may show plasmacytosis and eosinophilia. There is a lymphocytic and plasma cellular infiltrate in the alveolar septae and also around bronchi. The most florid form of lymphoid hyerplasia involving the lung in HIV infected children is known as polyclonal B-cell lymphoproliferative disorder (PBLD).

BRAIN FINDINGS WITH AIDS:

The differential diagnosis of cerebral mass lesions in AIDS includes non-Hodgkin's lymphoma, toxoplasmosis and progressive multifocal leukoencephalopathy (PML). Lymphomas tend to be large single masses but may be infiltrative and ill-defined. They are usually of large lymphoid cell type or immunoblastic.

Toxoplasmosis often produces smaller multiple masses.

CMV and cryptococcosis usually do produce mass lesions and cryptococcosis most often produces meningitis without marked inflammation.

HIV infection of microglia and macrophages residing in the vrain leads to a bariety of changes and specific pathologic findings, particularly in patients with dementia. They include subacute HIV encephalitis, HIV leukoencephalopathy, microglial nodules and PML (progressive multifocal leukoencephalopathy).

OPPORTUNISTIC INFECTIONS:

Infections seen in association with AIDS usually present with more extensive organ involvement, disseminated to multiple organs with poor inflammatory response, decreased sensitivity to serologic testing and diminished response to antimicrobial agents.

THE MOST COMMON ORGAN SITES:

Lung, gastrointestinal tract, liver, lymph node, bone marrow, and brain.

Pneumocystis carinii with extensive pneumonia is the most common infection.

FUNGAL INFECTIONS:

Candidiasis usually appears as oral thrush and sometimes produces tracheobronchial or esophageal infection but it is rarely disseminated.

Cryptococcosis often involves lung and meninges.

MYCOBACTERIAL INFECTIONS:

mycobacterium tuberculosis unsually pulmonary infection produces poor granulomatous reaction.

Mycobacterium avium complex is more disseminated but usually involves lymphoreticular organs, typically lymph nodes, spleen and liver are involved. Histologically one sees nodular cirrhosis with macrophages stuffed with acid-fact bacilli.

TOXOPLASMOSIS:

It produces multiple acute and chronic abscesses in the brain but less common in other organs.

CMV:

CMV infection can involve any organ but most commonly involves lung and GI tract.

HERPES:

Herpes simplex infections appear as single or

grouped vesicles on the skin, oral cavity, esophagus or perianal region. Dissemination is uncommon.

NEOPLASMS WITH AIDS:

HODGKIN'S DISEASE:

The incidence of Hodgkin's disease among HIV positive patients is increased, although the increase is not as marked as that of non-Hodgkin's lymphoma in the United States. Hodgkin's disease may be more frequent among patients who become infected with HIV through intravenous drug use rather than through sexual transmission. In the United States the ratio of HIV associated non-Hodgkin's lymphoma to Hodgkin's disease is reported to be 11:1, whereas a study from Europe reported a ratio of 2:1.

A higher proprotion of HIV positive patients have Hodgkin's disease with mixed cellularity type and they usually hav widespread disease (stage III or IV) at the time of diagnosis with frequent bone marrow involvement. B Symptoms (fever, night sweats and weight loss) are usually present and overall prognosis is not favorable. However, some patients attain durable complete remissions.

NON-HODGKIN'S LYMPHOMA:

AIDS related lymphomas arise in polyclonal B-cell proliferation from diminished immunosurveillance with decreasing CD4 lymphocytes, destruction of follicular dendritic cells allowing B-cell clonal proliferation, chronic antigenic stimulation, EBV infection and cytokine deregulation. A monoclonal proliferation eventually arises from a single clone that has accumulated sufficient genetic abnormalities.

Patients heavily immunosuppressed by cyclosporine based regimen could develop post-transplantation lymphoproliferative disorder if infected with EBV. Serologic evidence of primary or reactivated EBV infection appears to be invariably present in patients with post-transplantation lymphoproliferative disorders (PTLD'S) or in patients with AIDS-related lymphoproliferative disorders. In nearly all the cases, immunophenotypic or genetic studies reveal evidence of EBV infection of B-lymphocytes.

The prognosis of PTLD is highly variable, difficult to predict in individual cases. In general, a better outcome has been associated with disease confined to lymph nodes or to a single organ, resectable GI tract disease, polymorphous histology and polyclonality. Close follow-up of the patients are indicated because they can develop a high-grade B-cell lymphoma with high mortality rate.

Non-Hodgkin's lymphomas with AIDS usually appear as multifocal and multicentric tumor masses, GIT, liver, lungs, and brain most often affected. Lymph node and bone marrow involvement are much less frequent. About one-third are classified as small non-cleaved cell lymphoma (Burkitt or Burkitt-like). The second category about two-thirds of systemic lymphoma is best termed as diffuse non-cleaved large cell lymphoma and immunoblastic lymphoma. In both categoriesd often the neoplastic cells are infected with EBV.

KAPOSI'S SARCOMA:

A human herpes virus-like agent (human herpes virus 8) has been identified in skin lesion of Kaposi's sarcoma in both classic and AIDS-associated forms as well as in Kaposi's sarcoma of HIV negative homosexual men. The Agent appears to sexually transmit independently of HIV. Although the skin is involved in over 75% of cases and is often the site of initial presentation, visceral Kaposi's sarcoma mainly involves lungs, lymph nodes, and GI tract.

REPORTS:

CASE 1:

42 - year - old man presented with a right preauricular mass. Left side also appears slightly swollen. Patient is otherwise asymptomatic and says he is not high risk for HIV.

The biopsy of the preauricular mass revealed lymphoepithelial cyst and patient proved to be HIV-positive.

CASE 2:

68-year-old grandfatehr comes with chronic

diarrhea for 3-4 moths. Clinical diagnosis of ulcerative colitis. Endoscopy was done.

Colonic bipsy revealed colitis with CMC inclusion bodies in the histiocytes and endothelial cells in the lamina propria. Patient proved to have AIDS and several months later died of systemic infection.

CASE 3:

34-year-old man totally asymptomatic suddenly presented with shortness of breath and respiratory distress. Was admitted to ICU and died.

The patient proved to have AIDS and the autopsy showed multisystemic infections including toxoplasma encephalitis.

CASE 4:

55-year-old man with known diagnosis of AIDS developed non-tender cervical lymphadenopathy of several months duration.

Lymph node was excised and showed polyclonal lymphoproliferative disorder and the B lymphocytes were infected with EBC. Patient is still alive. no other lymphadenopathy or organ involvement after two years of follow-up.

CASE 5:

48-year-old female with known diagnosis of AIDS of several years duration developed cervical lymphadenopathy.

The lymph node was removed and showed Hodgkin's disease of mixed cellularity type.

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