Virology

Lec (2)

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Teaching Objectives:

1. Know different methods for escape from immune system.
2. Recognize the mechanism of diagnosis.
3. List methods of treatment and prevention.

Explain why infection with HIV leading to the death of helper T cells.

- The first mechanism, the virus bind with CD4 receptor and leading to death of cell
- The second mechanism, HIV acts as a "super antigen" which indiscriminately activates many helper T cells and leads to their demise.

Why some person has protection against HIV?

- In 1995, it was reported that a group of HIV-infected individuals has lived for many years without opportunistic infections and without a reduction in the number of their helper T (CD4) cells. The strain of HIV isolated from these individuals has mutations in the nef gene, indicating the importance of this gene in pathogenesis. The Nef protein decreases class I MHC protein synthesis, and the inability of the mutant virus to produce functional Nef protein allows the cytotoxic T cells to retain their activity.
- Another explanation why some HIV-infected individuals are long-term "non progressors" may lie in their ability to produce large amounts of alph-defensins. alph-Defensins are a family of positively charged peptides with antibacterial activity. In 2002, they were shown to also have antiviral activity. They interfere with HIV binding to the CXCR4 receptor and block entry of the virus into the cell.
- In addition to the detrimental effects on T cells, abnormalities of B cells occur. Polyclonal activation of B cells is seen, with resultant high immunoglobulin levels. Autoimmune diseases, such as thrombocytopenia, occur.

HIV has three main mechanisms by which it evade the immune system.

(1) Integration of viral DNA into host cell DNA, resulting in a persistent infection.

(2) High rate of mutation of the env gene.

(3) The production of the Tat and Nef proteins that down regulate class I MHC proteins required for cytotoxic T cells to recognize and kill HIV-infected cells.

The ability of HIV to infect and kill CD4-positive helper T cells further enhances its capacity to avoid destruction by the immune system.

Clinical Findings

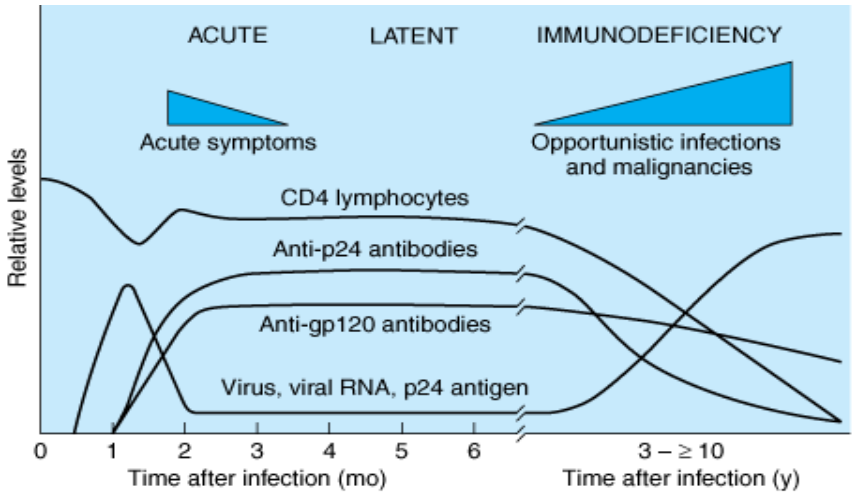
The clinical picture of HIV infection can be divided into three stages:

1- Early, acute stage.

2- Middle stage (Latent stage).

3- Late or immunodeficiency stage.

In the acute stage, which usually begins 2-4 weeks after infection, a mononucleosis-like picture of fever, lethargy, sore throat, and generalized lymphadenopathy occurs. A maculopapular rash on the trunk, arms, and legs (but sparing the palms and soles) is also seen. Leukopenia occurs, but the number of CD4 cells is usually normal. A high-level viremia typically occurs, and the infection is readily transmissible during this acute stage. This acute stage typically resolves spontaneously in about 2 weeks. Resolution of the acute stage is usually accompanied by a lower level of viremia and a rise in the number of CD8-positive (cytotoxic) T cells directed against HIV. Antibodies to HIV typically appear 10–14 days after infection.



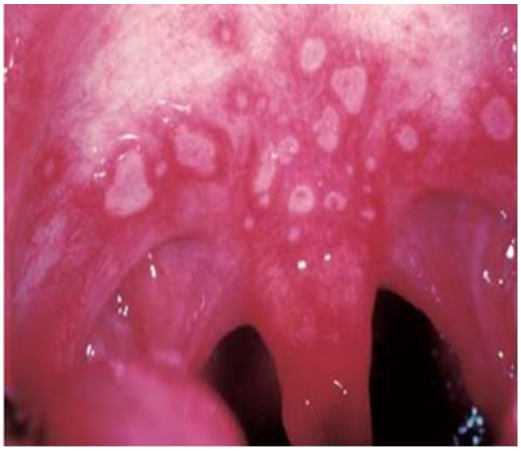
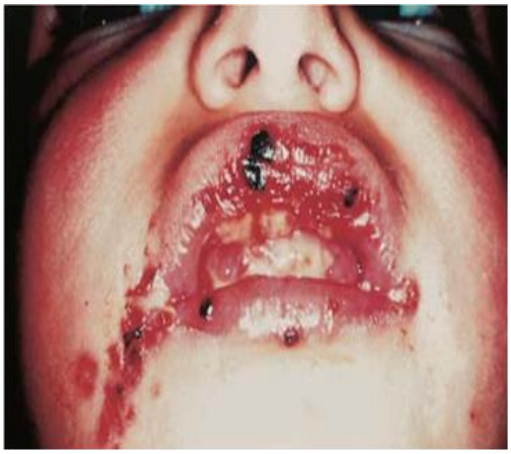
2- In the middle stage, a long latent period, measured in years, usually ensues. In untreated patients, the latent period usually lasts for 7-11 years. The patient is asymptomatic during this period. Although the patient is asymptomatic and viremia is low or absent, a large amount of HIV is being produced by lymph node cells but remains sequestered within the lymph nodes. This indicates that during this period of clinical latency, the virus itself does not enter a latent state.

3- Late stage or called AIDS-related complex (ARC) can occur during the latent period. The most frequent manifestations are persistent fevers, fatigue, weight loss, and lymphadenopathy. ARC often progresses to AIDS. The late stage of HIV infection is AIDS, manifested by a

decline in the number of CD4 cells to below 400/μL and an increase in the frequency and severity of opportunistic infections.

Table . Common Opportunistic Infections in AIDS Patients.

Site of Infection	Disease or Symptom	Causative Organism
Lung	1. Pneumonia	*Pneumocystis carinii,* cytomegalovirus
	2. Tuberculosis	*Mycobacterium tuberculosis*
Mouth	1. Thrush	*Candida albicans*
	2. Hairy leukoplakia	Epstein-Barr virus
	3. Ulcerations	Herpes simplex virus-1, *Histoplasma capsulatum*
Esophagus	1. Thrush	*Candida albicans*
	2. Esophagitis	Cytomegalovirus, herpes simplex virus-1
Intestinal tract	Diarrhea	*Salmonella* sp., *Shigella* sp, cytomegalovirus, *Cryptosporidium parvum, Giardia lamblia*
Central nervous system	1. Meningitis	*Cryptococcus neoformans*
	2. Brain abscess	*Toxoplasma gondii*
	3. Progressive multifocal leukoencephalopathy	JC virus
Eye	Retinitis	Cytomegalovirus
Skin	1. Kaposi's sarcoma	Human herpesvirus 8
	2. Zoster	Varicella-zoster virus
	3. Subcutaneous nodules	*Cryptococcus neoformans*
Reticuloendothelial system	Lymphadenopathy or splenomegaly	*Mycobacterium avium* complex, Epstein-Barr virus

Laboratory diagnosis.

2- The presumptive diagnosis of HIV infection is made by the detection of antibodies by ELISA. Because there are some false-positive results with this test. The definitive diagnosis is made by Western blot analysis, in which the viral proteins are displayed by acrylamide gel electrophoresis, transferred to nitrocellulose paper (the blot), and reacted with the patient's serum. If antibodies are present, they will bind to the viral proteins (predominantly to the gp41 or p24 protein). Enzymatically labeled antibody to human IgG is then added. A color reaction reveals the presence of the HIV antibody in the infected patient's serum.

3- The polymerase chain reaction is a very sensitive and specific technique that can be used to detect HIV DNA within infected cells.

4- The amount of viral RNA in the plasma (i.e., the viral load) can also be determined using PCR-based assays.

5- Ora-Quick is a rapid screening immunoassay for HIV antibody that uses a blood sample obtained by finger prick. Results require confirmation by a western blot test.

Treatment.

A-Nucleoside inhibitors.

1-Azidothymidine (AZT, Zidovudine) this drug causes chain termination during DNA synthesies. It is particularly effective against DNA synthesis by reverse transcriptase of HIV and inhibits growth of the virus in the cell culture. Other drugs that have a similar mode of action and used to treat patients with AIDS who are intolerant or resistant to AZT.

2- Dideoxyinosine
3- Dideoxycytidine (Zalcitabine, DDC)
4-Stavudine (zerit, d4T)
5-Lamivudine
6- Tenfovir

B-Non-nucleoside inhibitors.

These drugs are not cause chain termination but binding with reverse transcriptase and inducing a conformational change that inhibits the synthesis of viral DNA
1-Nevirapine (viramune) is usually used in combination with AZT and didnosine
2-Delavirdine

3-Efavirenz

- The current treatment of choice for advanced disease is a regimen consisting of two nucleoside inhibitors (zidovudine and lamivudine) and a protease inhibitor (indinavir). This combination is known as **HAART**, which is an acronym for "highly active antiretroviral therapy." It is very effective in prolonging life.

Vaccination.

-Whole virus vaccines: Attenuated, killed, defective.
-Subunit vaccines: monovalent or multivalent.
-Target cell protection: e.g. Abs to viral attachment route in or to CD4 receptor.
-Antigen presentation options: e.g. nonspecific immunostimulation.

1-**Scientists unveil promising new HIV vaccine strategy**
Date: November 26, 2018-**Source:**Scripps Research Institute
A new candidate HIV vaccine surmounts technical hurdles that stymied previous vaccine efforts, and stimulates a powerful anti-HIV antibody response in animal tests. The new vaccine strategy is based on the HIV envelope protein, Env. This complex, shape-shifting molecule has been notoriously difficult to produce in vaccines in a way that induces useful immunity to HIV**.**

Recently some scientists were developed two types of antibody 3BNC and 117 1074-10 specific for HIV, So this antibody give good result after tested on 9 volunteers due to interact with external antigen.

Control measures.

-Eliminate the high risk factors.
-Screening of blood.

Health education through.

-Avoid illegal sex.
-Avoid sharing needles or syringes.
-HIV infected mother should avoid breast-feeding.

First December consider as AIDS world awareness day.