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Euro Virology 2019: HIV Infection and its complications from pathologist's point of view- Vsevolod A Zinserling- Saint-Petersburg University, Russia

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The human immunodeficiency viruses (HIV) are two species of Lentivirus (a retrovirus subgroup) infecting human. Over time, they induce acquired immunodeficiency syndrome (AIDS), a disorder in which progressive immune system dysfunction allows opportunistic life-threatening infections and cancers to grow. Without treatment, the average survival time after HIV infection, depending on the HIV subtype, is estimated at 9 to 11 years. In most cases, HIV is a sexually transmitted infection which occurs by saliva, preejaculate, semen, which vaginal fluid touch or transfer. Research has shown (for both same-sex and opposite-sex couples) that if the HIV-positive partner has a consistently undetectable viral load, HIV is intransmittable through condomless sexual intercourse. Non-sexual transmission can occur during pregnancy from an infected mom to her baby, during childbirth through exposure to her blood or vaginal fluid, and through breast milk. HIV infects critical cells in the human immune system, such as aid T cells (specifically CD4 + T cells), macrophages and dendritic cells. HIV infection contributes to low levels of CD4 + T cells through a variety of mechanisms, including pyroptosis of abortively infected T cells, apoptosis of non-infected bystander cells, direct viral killing of infected cells, and killing of infected CD4 + T cells by CD8 + cytotoxic cells. When CD4 + T cell numbers decline below a critical level, cell-mediated immunity is lost, and the body is gradually becoming more susceptible to opportunistic infections, leading to AIDS growth. HIV belongs to the genus Lentivirus, part of the Retroviridae family. Lentiviruses have much in common with morphologies and biological properties. Many animals are infected with lentiviruses which are characteristically responsible for long-lasting diseases with a long duration of incubation. Lentiviruses are transmitted as enveloped, single-stranded, positive-sense RNA viruses. Upon entry into the target cell, a virally encoded enzyme, reverse transcriptase, which is transported along with the viral genome in the virus particle, transforms the viral RNA genome (reverse transcribed) to double-stranded DNA. The resulting viral DNA is then imported into the cell nucleus, and a virally encoded enzyme, integrase, and host co-factors are integrated into the cellular DNA. Once integrated, the virus may become latent, allowing for an indeterminate amount of time for the virus and its host cell to avoid immune system detection. The HIV virus can remain dormant in the human body for up to 10 years after primary infection; the virus does not cause any symptoms during this period. Alternatively, it is possible to transcribe the integrated viral DNA, generating new RNA genomes and viral proteins using host cell resources that are packaged and released from the cell as new virus particles that will start the replication process again. For example, less than 1 per cent of Africa's sexually active urban population was measured in 2001, and this proportion is even smaller in rural communities. In addition, only 0.5 per cent of pregnant women attending urban health facilities were notified, screened or obtained their test results in 2001. Again, in rural health facilities, the proportion is even lower. Therefore, donor blood and blood products used in medicine and medical research are routinely screened for HIV, as donors may be unaware of their infection. HIV-1 testing is initially performed using an immunosorbent enzyme-linked assay (ELISA) to detect HIV-1 antibodies. Unless new exposure to an infected partner or partner of unknown HIV status has occurred, specimens with a non-reactive result from the initial ELISA are considered HIV-negative. Specimens with a product of reactive ELISA are retested in duplicate.

HIV infection remains one of the most dangerous diseases and important causes of death. Numerous investigations are devoted to problems of epidemiology, molecular biology, treatment, psychology etc. The number of studies discussing the results of pathological studies is very limited. Having long term experience in HIV pathology, we can formulate the following items. Most important questions to be studied on the autopsies

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of the deceased from HIV-infection: exact list of secondary infections and tumors with specification of their localization; evaluation of the efficacy of treatment; revealing of immediate death cause; collection of specimen for further investigations in order to study the mechanisms of the disease and its complications. Methods recommended for postmortem investigation are detailed histological study of all macroscopically changed and not changed organs with use of certain special staining; bacteriological and mycological investigation of all suspected lesions in order to clarify their etiology and certain properties of the pathogens; different virological, molecular-biological methods and immunohistochemistry in order to study the localization of lesions due to HIV and other viruses and some of their properties. Among the most interesting, important and not sufficiently known changes we pay special attention to the brain. We have to distinguish direct and indirect lesions due to HIV virus itself, other pathogens (CMV, Toxoplasma, Cryptococcus, HSV, JCV, EBV first of all) and other influences and follow up them in different decades of epidemics. Some clinico-pathological correlations in perinatal HIV: viral load in pregnant women correlated with the depth of immunosuppression; women without antiretroviral treatment had more expressed grade of immunosuppression; frequency of secondary purulent inflammation correlated with the grade of immunosuppression. Main probable pathogenic mechanisms of Placenta lesion in HIV: direct lesions of placenta macrophages (Hofbauer cells), endotheliocytes and decidual cells with development of typical changes of nuclei, leading role in inflammatory reaction of CD14+ in comparison with CD68+ cells; disturbance of angiogenesis due to hyper expression of anti-angiogenic factor TGF?; probable disturbances of syncytial-capillary membrane. Main questions for further investigations: clarifying incidence and etiology of placenta inflammation and intrauterine infections in women with HIV; further studies of mechanisms of placenta lesions in HIV infected women; clinico-pathological correlations between morphological changes in placenta and outcome of pregnancy versus antiretroviral treatment; Clinico-pathological correlations between symptoms in children from HIV-infected mothers and post-mortem histology; studying impact of prenatal infections on development of children and morbidity of teenagers and adults. Question for the life-time pathological and cytological diagnostics are study of smears or liquid biopsies of cerebrospinal fluid for evaluating mycobacterium, cryptococci and tumour cells, lymph node biopsies in order to identify the origin of their lesion, needle biopsies of other organs due to clinical necessity.

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