

Late diagnosis of HIV-infection

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Late diagnosis of HIV-infection is defined as diagnosis of HIV in a stage, where immunodeficiency is advanced or clinical progression has already occurred or is imminent. Immunodeficiency is considered to be advanced with any CD-cell count below 200/mcl. In different case series, clinical manifestations have been defined differently, either to be present at diagnosis of HIV-infection or imminent within 3 -12 months.

Late diagnosis of HIV-infection is still frequent, although its rate is declining in several cohorts. In different studies 30% of HIV-infections are considered to be diagnosed late.

Risk factors have been analysed and found to be very young or older age, female sex, to be migrant and to have no known or acknowledged risk factor for HIV-infection.

Clinical consequences of late HIV-diagnosis are well known. The rates of viral suppression achieved are lower in patients with advanced immunodeficiency, the rates of clinical progression even if antiretroviral therapy is initiated is higher, the rates of adverse effects of drugs are higher, mortality is higher and with concurrent opportunistic infections the risk of additive toxicity or drug-drug interactions is higher.

The question whether antiretroviral therapy (ART) can be initiated safely and effectively with concurrent opportunistic infections is still open, for short-term therapies many doctors would rather treat first opportunistic infections and then initiate ART in a stabilised clinical situation. For opportunistic diseases, where therapy has to be given for a longer time period, e.g. tuberculosis, the situation is different. To delay the initiation of ART until tuberculostatic therapy can be stopped may pose patients at risk for further clinical progression. Therefore ART should be initiated during Tb-treatment in patients with CD-4-cell counts below 200/mcl, although with an interval of several weeks between the start of both therapies.

One of the frequent problems in patients with late HIV-infection is the immune reconstitution inflammatory syndrome (IRIS). It is defined as the clinical worsening of any pre-existent condition with the onset or shortly after the onset of ART, in most cases as an inflammatory flare of the given disease. The pathogenesis of IRIS is poorly defined; whether IRIS represents enhanced or lowered adaptive immune response or an imbalance between the reconstitution of innate and adapted immunity is currently been evaluated. IRIS occurs in 20-30% of cases of late HIV-infection and can be based on a large group of diseases, e.g. mycobacterial infections, hepatitis B, herpesvirus infections but as well on Graves' disease and other autoimmune conditions. Risk factors for IRIS are young age and low CD-4-cell count.

The management of IRIS can be challenging and in some cases can necessitate the use of corticosteroids.

Suggested References for Further Reading

1. Chadborn TR, Delpech VC, Sabin CA, Sinka K, Evans BG. The late diagnosis and consequent short-term mortality of HIV-infected heterosexuals (England and Wales, 2000-2004). *Aids* 2006;20(18):2371-9.
2. Delpierre C, Dray-Spira R, Cuzin L, et al. Correlates of late HIV diagnosis: implications for testing policy. *Int J STD AIDS* 2007;18(5):312-7.
3. French MA. Disorders of immune reconstitution in patients with HIV infection responding to antiretroviral therapy. *Curr HIV/AIDS Rep* 2007;4(1):16-21.
4. Girardi E, Aloisi MS, Arici C, et al. Delayed presentation and late testing for HIV: demographic and behavioral risk factors in a multicenter study in Italy. *J Acquir Immune Defic Syndr* 2004;36(4):951-9.
5. Longo B, Pezzotti P, Boros S, Urciuoli R, Rezza G. Increasing proportion of late testers among AIDS cases in Italy, 1996-2002. *AIDS Care* 2005;17(7):834-41.
6. Manavi K, McMillan A, Ogilvie M, Scott G. Heterosexual men and women with HIV test positive at a later stage of infection than homo- or bisexual men. *Int J STD AIDS* 2004;15(12):811-4.
7. Mugavero MJ, Castellano C, Edelman D, Hicks C. Late diagnosis of HIV infection: the role of age and sex. *Am J Med* 2007;120(4):370-3.
8. Schwarcz S, Hsu L, Dilley JW, Loeb L, Nelson K, Boyd S. Late diagnosis of HIV infection: trends, prevalence, and characteristics of persons whose HIV diagnosis occurred within 12 months of developing AIDS. *J Acquir Immune Defic Syndr* 2006;43(4):491-4.