

THE CONCOMITENT INFECTION WITH MYCOBACTERIUM AND AIDS – A HEALTH PROBLEM FOR IMUNODEPRESSED PATIENTS

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Abstract

This study makes concrete references at the 22 children hospitalised in the Clinical Hospital of Infectious Diseases from Oradea with HIV-infection (AIDS) in different forms. Seven of this children presented concomitant, different forms of tuberculosis caused by Mycobacterium tuberculosis, hospitalised in the Clinical Hospital of Ftiziology Diseases from Oradea.

Key words: Mycobacterium tuberculosis, bovis, immunodepression

INTRODUCTION

Mycobacterium bovis is a slow-growing (16 to 20 hour generation time), aerobic bacterium and the causative agent of tuberculosis in cattle (known as bovine TB). Related to *M. tuberculosis*—the bacteria which causes tuberculosis in humans—*M. bovis* can also jump the species barrier and cause tuberculosis in humans. (Harrison's, 2001), (Bell E., 2005), (Murray P.R., Rosenthal K.S., Pfaller M.A., 2005).

M. bovis is usually transmitted to humans via infected milk, although it can also spread via aerosol droplets. Actual infections in humans are rare, mostly due to pasteurisation killing any bacteria in infected milk; as well, cattle are randomly tested for the disease and immediately destroyed if infected. However, in areas of the developing world where pasteurisation is not routine, *M. bovis* is a relatively common cause of human tuberculosis. (Wooldridge K., 2009).

In the last ten years (1998-2008) an increase in the pulmonary and extra-pulmonary tuberculosis is recorded globally in the population, but especially in case of the immunodepressed hosts to which positive-HIV patients belong to. In 1993 tuberculosis was included among the diseases that can indicate AIDS and globally it is considered the most frequent opportunistic infection. (Arnvig K.B., Young D.B., 2009).

It is accepted that the incidence of tuberculosis is of 500 times higher in the case of AIDS patients in comparison with the general population, an increase in prevalence for the positive HIV patients with multi-resistant strains being recorded. (Cole et al., 1998), (Camus J.C., et al. 2002). Tuberculosis can appear in any stage of HIV infestation, but it

presents clinical-evolutional characteristics according to the degree of immunodepression. (Madigan M., Martinko J., 2005).

The sero-prevalence studies in the countries where tuberculosis and HIV are spread, suggest that the relative risk of active tuberculous disease in children infected with HIV is of 5-10 times higher in comparison with the sero-negative children. The explanation could be the essential role played by the lymphocytes CD4, in the immune response against *Mycobacterium tuberculosis*. (Murray P.R., 2005), (Livny J., et al., 2006), (Rebedea I., 2000).

In the same time, it can be noticed the accelerated progression of HIV in the patients with active tuberculosis as a consequence of the immune stimulation and of the increase of cytokines determined by the *Mycobacterium tuberculosis*, causing the increase of the viral replication. (Ryan K.J., 2004), (Bell E., 2005), (Flowers T., 1995).

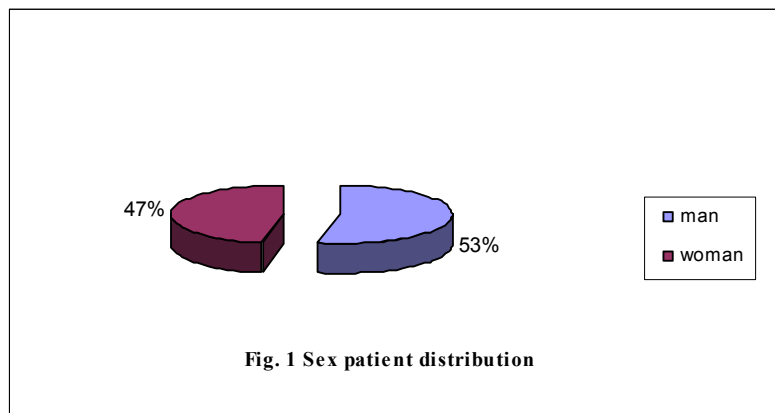
MATERIAL AND METHODS

It was accomplished a study on a lot of 22 children having the age between 0-18, found in the records of the Clinical Hospital of Infectious Diseases from Oradea with the diagnosis of HIV in different stages. Seven of these cases have presented different forms of tuberculosis monitored by the Clinical Hospital of Phtysiology Disease from Oradea.

RESULTS AND DISCUSSIONS

It must be taken into account the diagnosis of tuberculosis, because sometimes it is neglected for the bacterial etiology or with *Pneumocistis carinii* in the context of immunodepression.

There weren't recorded significant differences regarding the sex of the patients in the 20 studied cases. (Figure 1).



The cutaneous test to tuberculin is difficult to be interpreted due to the reduced reactivity through immunodepression, but a positive test is very useful. In our lot, testing was positive with 2u PPD in three cases (42%) and with 10u PPD in two cases (28%). This testing will be practiced for all the sero-positive children exposed to a source of Koch bacillus. An induration of over 5 mm is considered positive. (Reddy JR. Et all., 2002).

The clinical manifestations consist in fever, cough, adenopathy, nocturnal transpiration and weight loss. As long as the immunodepression is more obvious, there is a tendency to atypical manifestations (clinical-radiological). When $CD\ 4 > 350/mm^3$, the clinical manifestations are similar to a reactivation of the infection in the immunocompetent host.

The radiological changes include focal condensations in the superior and hilar lobes, multilobar condensation, interstitial infiltrates and hilar adenopathy cavities.

In the atypical forms, some multiple injuries can appear that don't have a classical apical placement, evolving rarely to excavation, hilar adenopathy without parenchymatous infiltrate, pulmonary infiltrate diffused in the median-pulmonary or inferior area.

The extrapulmonary tuberculosis is more frequent in children with HIV, being frequently associated with the pulmonary tuberculosis, being the appanage of the advanced forms of immunodepression ($CD\ 4 < 200/mm^3$).

The bacteriologic diagnosis is based on the highlight of Koch bacillus on a direct smear or in cultures on Lowenstein- Jensen or BACTEC medium. In the pulmonary tuberculosis some samples of saliva, tracheal aspirate, broncho-alveolar lavage, pulmonary biopsy, and gastric aspirate were taken.

In the extrapulmonary tuberculosis, some probes are sampled for tracking the Koch bacillus in the blood, marrow, lymphatic nodules, LCR, etc.

In the severe forms of immunodepression, non-tuberculous Mycobacteria are frequent in the children with positive HIV, for this reason, a smear with positive result is not sufficient for the diagnosis of tuberculosis. For this reason, we underline the importance of the culture, not only for the diagnosis, but also for the determination of the sensibility to tuberculostatics, the chemical resistance being frequently encountered.

The bacteriological test, in the situations studied by us, highlighted a Koch positive bacillus at the microscopic examination in 5 cases (71%) and the cultures were positive in 4 cases (57%)

No optimum scheme for the treatment of tuberculosis in sero-positive children was established.

The American Academy for Pediatrics recommends a total duration of the treatment of 12 months, and the CDC recommendation is that of 6 months of treatment, but with the possibility of its extension in the case of a satisfactory clinical-radiological response.

Because Koch bacillus is resistant to HIN (hydrazide) with a rate of 4%, it is recommended as in the case when the sensibility of Koch bacillus to tuberculostatics is unknown, streptomycin and etambutol to be induced in the initial treatment. In the disseminated cases, streptomycin is recommended for 2 months in the initial regime, the treatment being continued for other 10 more months with biotherapy. If the initial regime doesn't contain hydrazide and rifampicine, the treatment will be prolonged for 18 months.

In the cases under study (6 cases), the primo-infection with hilar adenopathy was treated with HIN+RMP+PZA 6/7 for two months, followed by INH+RMP 2/7 for four months.

A case that presented a nodular infiltrant form received the same treatment scheme with favorable evolution. No cases with disseminated cases and no forms resistant to treatment were recorded.

A case with repeated bacterial super-infections received the above-mentioned scheme for two months, then INH+PZA for four months 2/7, followed by INH 2/7 for three months. In the case of INH 2/7, it was recorded a reactivation during which INH+EMB was administered for three months.

In the case of the tuberculostatics, hepato-protective medication (Vitamin B₆, Silimarina) was administered continuously having in view the hepato-protective action of these medicines.

Concomitantly with the tuberculostatics, the children also received antiretroviral medication with 2 INRT+1 INNRT, fact that represented an accumulation of adverse reactions, but the interruption of the treatment was not necessary.

Two cases with reduced compliance to the treatment were recorded, but the administration of the medication was made under strict supervision.

Under a correct treatment, it was noticed that the presence of the HIV infection doesn't aggravate the form of tuberculosis, and that the treated tuberculosis doesn't influence significantly the evolution of the HIV infection.

The evolution was favorable in the six cases of primo-infection with hilar and ondulant adenopathy in the case of a nodular-infiltrative pulmonary tuberculosis with repeated bacterial super-infections.

No deaths were recorded.

CONCLUSIONS

- tuberculosis is a frequent infection in the positive HIV patients with etiological (*Mycobacterium tuberculosis* or *Atipic Mycobacterium*), clinical and diagnostic characteristics according to the degree of immunodepression (the more advanced the immunodepression, the more frequent the forms of atypical diseases).
- Tuberculinic examination has the value of screening, the positive response being very important in establishing the diagnosis. It can be negative in advanced stages of immunodepression, for this reason, it will be systematically correlated with the radiological test.
- Bacteriological examination is useful for both the diagnosis of the pulmonary and extrapulmonary tuberculosis, and the culture offers the possibility to determine the sensibility to tuberculostatics.

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