Immunocompromised Host: from the Early Events until the Impact of Acquired Immunodeficiency Syndrome

Sylvio Celso Gonçalves da Costa

Laboratório de Imunomodulação, Departamento de Protozoologia, Instituto Oswaldo Cruz, Av. Brasil 4365, 21045-900 Rio de Janeiro, RJ, Brasil

The concept that microorganisms can modulate the host resistance was historically reviewed in the present article. The importance of African trypanosomiasis in the development of the research on immunosuppression as well as the impact of human immunodeficiency virus infection are discussed. Each day new opportunistich organisations establish a constant challenge for the correct diagnosis of concomitant infections in acquired immunodeficiency syndrome. The importance of parasite infection in the balance of host resistance in the third world was emphasized. Finally, some aspects of *Leishmania* as opportunistich organisms were presented.

Key words: immunocompromised host - acquired immunodeficiency syndrome-Aids - human immunodeficiency virus-HIV

The idea that microorganisms can modulate the host resistance is well known at longtime ago. Chanfort reported in its “maxims” that patients with paludism were partially protected against the pest. And long, long time before the Egyptians had observed empirically that people presenting abscess had become more resistant to epidemic incidents than health ones. In these cases infection promotes immunostimulation but it was also observed that some infections can induce immunosuppression. The notion that infection could induce immunosuppression was brought out chiefly by observations on African trypanosomiasis which induce profound suppression of the host immune system and led to the raise of opportunistic infections. It was observed in the early 20th century that patients suffering of sleeping sickness presented lobar pneumonia (Low & Castellani 1903). This was later investigated in patients with a generalized immunosuppression after *Trypanosoma* infection. It has been observed that this suppression can affected programs of vaccination in live-stock carrying out *T. vivax* and *T. congolensis* infection. This suppression is correlated with low antibodies to vaccines used in cattle.

In 1981 a report sent to the Centers for Disease Control (CDC) showed that in the past eight months, five cases of pneumonia due *Pneumocystis carinii* were diagnosed in Los Angeles. Normally this pneumonia was known as an opportunistic disease occurring in patients with cancer or in people treated with immunosuppressive drugs. This disease was extremely rare and treated with pentamidine, which was still considered to be an experimental drug. So, only with authorization from the CDC the drug could be distributed. This new fact called the attention of the CDC, since the patients were young homosexual people and in general their immune system was immunocompetent. In parallel, during a period of 30 months, 26 new cases of Kaposi sarcome were detected in young homosexual men in New York and California. Some of these patients also presented pneumonia due to *P. carinii* and other severe opportunistic infections. In January of 1983, new and well documented cases appeared among women maried to men that used injectable drugs, showing that the disease was not exclusive to males. Since the disease was transmitted by blood transfusion and sexual contact, the research groups were convinced that acquired immunodeficiency syndrome (Aids) was caused by an infectious agent. This hypothesis was confirmed by Luc Montagnier at Pasteur Institut by the isolation of human immunodeficiency virus (HIV) and brought a new impact to the biological and medical science by amplifying the spectra of immunocompromised hosts (Barre-Sinoussi et al. 1983, CDC 1986).

The malnourished host is another condition considered as acquired immune deficiency which exhibits many immunodeficiencies similar to those typically observed in Aids. As this occurs in many regions of the third world and in developing countries it contributes to aggravate HIV infection.
Some of these features include depressed cell-mediated immunity (mainly as a consequence of depressed T-cell number), complement deficiencies, reduced phagocytic and microbicidal as well as tumoricidal activities of macrophages.

This condition is overlapped by helminthic infections that are common in many regions of developing countries, which is estimated to affect more than 1.5 billion people. People highly infected with helminths in these regions have been proposed to explain a high level of tuberculosis (TB) reactivation (Beyers et al. 1996, Warren et al. 1996). Helminth appears as a potent agent to induce Th2 response which is expressed by high IgE levels. A direct correlation of high serum IgE levels and an incidence of high skin test tuberculin has been observed in some towns of South Africa (Beyers et al. 1998). Similar observation was made in patients suffering with cutaneous leishmaniasis caused by Leishmania braziliensis. In Rio de Janeiro this infection is more benign than those observed in other Brazilian towns. Self cure is admitted by some authors and low dose therapy has been propose with good results (Oliveira Neto et al. 1997). During an outbreak of cutaneous leishmaniasis in Rio de Janeiro patients presenting large lesions were frequently associated with high total IgE levels (Gonçalves da Costa et al. 1975). Nevertheless specific Leishmania IgE was described in infection by L. braziliensis but not on L. amazonensis (Affchain et al. 1983). It has been observed in Africa that faster progression to Aids occurred in highly endemic areas for helminths (Anzala et al. 1995) was associated with an increased plasma HIV viral load (Dyer et al. 1998). Increased plasma HIV viral load, considered the reliable marker of HIV infected patients (Mellors et al. 1996), is associated with leishmaniasis and decrease following its treatment (Wolday et al. 1998). It has been suggest that pre-treatment HIV viral load influences the response to anti-Leishmania chemotherapy and it was observed that active visceral leishmaniasis is correlated with increased viral replication, supporting the idea that concomitant infections plays an important role in disease progression of either infection (Berthe et al. 1999). In leishmaniasis the discussion is very stimulating since resistance to Leishmania infection is correlated with Th1 response. It has been shown that Th1 cells and particularly IFN-γ have a protective role in murine L. major infection; on the other hand Th2 cells and their products lead to disease progression (Titus et al. 1984, Heinzl et al. 1989). In many situation we can observe a transitory immunodepression as that one caused by the virus of rubella (Lafaix 1990). This virus can exacerbate a concomitant infection by L. major (Gonçalves da Costa, unpublished data).

It was shown that T-cell clones of Th1 or Th2 pattern from mice infected by L. major reacted with different antigenic fractions (Sadick et al. 1990). However attempts of vaccination have become a difficult task since host immune background in third world is turned to Th2 profile. This may explain little efficacy or lack of protection to TB by BCG vaccination in Africa and Asia prophylactic programs. HIV/Aids brings out the protozoan L. donovani and other species of Leishmania as opportunistic parasite. HIV, Leishmania sp. and Mycobacterium for example, which are parasite of immune cells present many common aspects chiefly characterized by the suppression of the host immune response, being the inducement of the Th1 suppression one of the most important mechanisms.

The cure and lesion healing lead to a premunition condition, since it is possible to isolate the parasite from scar ten years after healing (Oliveira Neto et al. 1997). HIV infection can reactivate either visceral (Badaró et al. 1986, Cortés et al. 1997) or cutaneous leishmaniasis (Machado et al. 1992). When Leishmania is analyzed as an opportunistic organism it presents many aspects to be considered; one of the most important is the dissemination of the infection. Co-infection with HIV lead to atypical forms of clinical presentation (Gradoni & Gramiccia 1994, Michiels et al. 1994). The association of different pathologies may occur as leishmaniasis, Kaposi’s sarcoma and Aids. It is interesting to emphasize that increased plasma HIV viral load has been observed in association with leishmaniasis and decreasing levels were observed after Leishmania treatment (Wolday et al. 1999).

Thus different mechanisms seem to favor HIV viral load in immunocompromised host: (a) inhibition of Th1 response by the induction of Th2 by helminths prior to HIV infection; (b) competition on the same Th pattern seems to be important for host resistance against HIV and other microorganisms during concomitant infection.

Opportunistic parasitoses have been diagnosed more and more often in most developing countries and polyparasitism become a field very attractive. Some opportunistic organisms as Microsporidia have been underestimated (Schottelius & Gonçalves da Costa 2000) and prevalence of this and other opportunistic microorganisms or parasites tends raised since accurate diagnostic methods will be applied.

Another point to be emphasize is that in children, disease outcome is usually faster and more serious than in adults, and high mortality rate due to serious opportunistic infections (Bernstein et al. 1989, Ortigão-de-Sampaio et al. 1999) in children in general is more affected by helminths. Polyparasitism can also interfere with immuno-
diagnostic tests either directly through cross-reactions or indirectly through its effect on immune system (Buck et al. 1978).

The prevalence of opportunistic parasitic infections has particularities in function of endemic problems of each region. Cryptosporidium and Isospora belli appear between the most frequent opportunistic parasitic infections in African patients with Aids (Henry et al. 1986, Pape et al. 1989, Datry 1989, Colebunders et al. 1998). The present workshop will show besides the general aspects of immunocompromised host, the situation of opportunistic parasitoses and mycoses in Brazil. Chagas disease appears in Latin America as an important opportunistic organism and presents frequent infection of central nervous system (Rocha et al. 1994). Reactivation of Chagas disease in immunocompromised patients outside Aids has been described either cancer or in organ transplantation (Mattosinho- França et al. 1969, Monteverde et al. 1976, Jost et al. 1977, Kodl et al. 1982, Rocha et al. 1994). The action of immunosuppressive drugs in American trypanosomiasis has been investigated in experimental model and many aspects has been correlated with the pathology observed in immunocompromised patients in which Chagas disease reactivation occur (Gonçalves da Costa & Calabrese et al. 1992, Calabrese et al. 1996, 2000, Calabrese 1999). It has been suggest that eradication of helminthic infections may have an important impact on Aids as well TB in developing countries (Bentwich et al. 1999) which will be a good program of investigation in our country. It was also emphasize many aspects of opportunistic mycobacterium species and host defense mechanisms.

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