Abstracts

Infections in Other Immunocompromised Hosts

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Ascaridiasis as a Risk Factor for Anemia in a Special Immunocompromised Host: The Pregnant Women


Background: From many points of view, the pregnant woman could be considered as a temporarily immunocompromised host due to immunosuppressive processes that prevent fetal rejection in utero. The increased susceptibility of pregnant women to different infections has long been recognized, but the magnitude of some diseases burden in this particular group, have only recently been the focus of research. Some of them are the tropical diseases such as infections due to helminths.

Objectives: We were interested on study the aetiological agents producing intestinal parasitosis as well their effects on clinical and hematological parameters, in a cohort of asymptomatic pregnant women living in endemic areas of Venezuela.

Methods: During 24 months, 1175 pregnant women attending 20 antenatal care centers from 10 states were included and evaluated. Routine prenatal control, physical examination and laboratory studies were performed (CBC, serological screening for HIV, HBV, Syphilis and Toxoplasmosis). Coproparasitological studies all women were done. Different stools examinations were used in detecting parasites. Uni- and multivariated analyses were made to assess risk factors. All data were analyzed with SPSS 10.0 at 95% confidence.

Results: Mean age and gestational age were 23.2±6.1 y-old and 29.9±3.8 weeks. Anemia was observed in 68.3% of woman, and eosinophilia in 25.1%. Intestinal parasitosis was seen in 899 women (76.5%). From this total, 62.7% corresponded to Ascaris lumbricoides, 37.4% to Trichuris trichiura, 22.55% to Giardia lamblia, among others; 50.7% presented infections due to two-four different parasite species. Anemia was significantly higher in A. lumbricoides infected women (89.9% vs. 31.9% in non-infected). Relative risk of anemia in women infected with A. lumbricoides was 2.81 (95%CI 2.45–3.23) (p<0.001). Relative eosinophils and relative lymphocytes counts were significantly higher in those infected compared with those woman non-infected.

Conclusions: Anemia has been frequently reported for other helminthes (i.e. hookworms) but rarely for A. lumbricoides which can be tissue dwelling or intestinal and induce a dramatic expansion of the Th2 lymphocyte subset. It remains unclear whether these Th2-derived responses, including IgE, eosinophilia and mastocytosis are important in the protective immune response to the parasite, or are responsible for immune-mediated pathology, or both. The implications of these results should be further studied and defined.

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Antifungal Prophylaxis is Effective against Murine Invasive Pulmonary Aspergillosis

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Background: Antifungal prophylaxis is a promising strategy to prevent and/or ameliorate invasive pulmonary aspergillosis (IPA). Concerns have arisen over the use of prophylactic voriconazole, so alternative antifungal strategies merit exploration. In particular, lipid amphotericin formulations are promising prophylactic agents because they accumulate in tissues, and thus may not require daily administration to mediate protection against the small numbers of inhaled conidia initiating infection.

Methods: BALB/c mice with cyclophosphamide/cortisone acetate-induced immunosuppression were infected via inhalation with A. fumigatus. Mice were treated iv prior to infection with AmBisome (LAmB), Abelcet (ABLC), amphotericin B (AmB),
Adenovirus Infections

Mouse Models for the pergillosis

Objectives: We investigated the contribution of the host's adaptive immune response and the efficacy of immunotherapy in the control of systemic adenovirus infections using two mouse models.

Methods & Results: Severe combined immune deficient (SCID) mice, intranasally inoculated with mouse adenovirus type 1 (MAV-1), develop a fatal disseminated disease characterized by hemorrhagic enteritis (Lenaerts et al., 2005, Antimicrob Agents Chemother 49, 4689-99). When SCID mice were treated with antisera containing MAV-1 specific IgG, MAV-1-induced death was significantly delayed from day 18 p.i. (untreated mice) to day 42-60 p.i. (antiserum-treated mice). The extent of the delay was dependent on the titer of MAV-1 neutralizing antibodies in the antiserum. The MAV-1 antiseras were obtained from immunocompetent mice challenged with MAV-1 and were transferred to the MAV-1-infected SCID mice at day -1 and day 9 post infection. Ultimately, MAV-1-infected SCID mice treated with the MAV-1-antisera showed 100% mortality, with identical pathology and similar virus titers in the target organs as seen in untreated, infected SCID mice. These results indicate that antibodies play a major role in protection and elimination of systemic adenovirus infection. In an alternative mouse model for adenovirus infection, cyclophosphamide (CY) was administered to adult BALB/c mice to induce a general and reversible immunosuppression. MAV-1-related mortality correlated with the duration of immunosuppressive therapy. Mice receiving CY for 3 or more weeks succumbed to an identical pathology and similar virus titers in the affected tissues as seen with MAV-1-infected SCID mice. On the contrary, mice in which immunosuppressive therapy was ceased 1 week post infection did not develop symptoms and survived. These mice showed high serum titers (≥1:160) of MAV-1 neutralizing antibodies. Studies are ongoing to evaluate the efficacy of antiviral agents such as cidofovir) in this MAV-1/CY model.

Conclusions: These two new mouse models will increase our understanding of the suppression of adenovirus disease by antiviral and/or immunotherapy and will be helpful in the development of an adequate treatment for systemic adenovirus infections in immunocompromised patients.

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Mouse Models for the Evaluation of Antiviral and Immunotherapy in the Treatment of Systemic Adenovirus Infections

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Background: Severe adenovirus infections are of increasing concern in AIDS patients and transplant recipients under immunosuppressive therapy. Unfortunately, current therapeutic modalities for adenovirus infections are limited.

Objectives: We investigated the contribution of the host’s adaptive immune response and the efficacy of immunotherapy in the control of systemic adenovirus infections using two mouse models.

Methods & Results: Initially, we compared the efficacy of a single dose of LAmB at 15 mg/kg to a dual treatment dose of 7.5 mg/kg given every other day. The single 15 mg/kg dose and the second of the dual 7.5 mg/kg doses were administered 24, 48 or 72 hours prior to infection. Only administration of dual 7.5 mg/kg doses of LAmB at 24 or 48 h prior to infection resulted in equivalent, significant protection as compared to placebo (100% vs 50%, p <0.05).

This data indicated that the total amount of LAmB administered over time was more important than the individual amount of each dose. Next, we compared dual doses of LAmB at 7.5 mg/kg with ABLC at 7.5 mg/kg, AmB at 1 mg/kg, and CAS at 1 mg/kg given on days -4 and -2 prior to infection. Additionally, CAS was also administered as a single dose 6 hours prior to infection. Only LAmB and the single dose arm of CAS significantly improved survival compared to placebo (75% and 88% vs 25% survival of placebo, p <0.04).

Lung CFUs was significantly reduced by prophylactic administration of LAmB (p=0.005), AmB (p=0.03), or CAS (given 6 h prior to infection, p=0.0002) but not ABLC. These results were mirrored in histopathological evaluation since lungs from mice receiving placebo and ABLC revealed large amounts of elongated hyphae with moderate necrotizing pneumonia, whereas lungs of mice treated with LAmB, AmB, or CAS did not.

Conclusions: These data indicate that LAmB administered daily or every other day is a promising candidate for prophylaxis against pulmonary aspergillosis in neutropenic hosts. CAS also mediates prophylactic effect, but must be dosed more often than LAmB for efficacy.

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Strategy of Vaccination Against HBV-infection in Hemodialysis Patients with 'Isolated' HBCAb

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Background: Advisability of vaccination against the HBV infection in patients with 'isolated' HBCAb...