Hindawi Publishing Corporation
Mediators of Inflammation
Volume 2015, Article ID 430525, 10 pages
http://dx.doi.org/10.1155/2015/430525

Research Article

Resistance to *P. brasiliensis* Experimental Infection of Inbred Mice Is Associated with an Efficient Neutrophil Mobilization and Activation by Mediators of Inflammation

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Received 3 July 2015; Revised 21 October 2015; Accepted 25 October 2015

Academic Editor: Helen C. Steel

Paracoccidioidomycosis (PCM) is a systemic fungal infection, endemic in Brazil, that leads to severe morbidity and even mortality if not correctly treated. Patients may respond differently to PCM depending on the pattern of the acquired immune response developed. The onset of protective immune response is notably mediated by neutrophils (PMN) that play an important role through directly killing the fungi and also by interacting with other cell types to modulate the acquired protective immune response that may follow. In that way, this study aimed to present and compare different experimental models of PCM (intraperitoneal and subcutaneous) regarding PMN production and maturation inside femoral bone marrow and also PMN infiltration in peritoneal and subcutaneous exudates of resistant and susceptible mice. We also assessed the fungal colony forming units and the levels of soluble inflammatory mediators (LTB4, KC, IFN-γ, GM-CSF, and IL-10) inside subcutaneous air-pouches to compare the efficiency of the PMN present at this site in relation to the two main neutrophil functions: initial lysis of the invading pathogen and modulation of the acquired immune response. *P. brasiliensis* inoculated intraperitoneally was able to disseminate to the bone marrow of susceptible mice, causing a more marked alteration of PMN production and maturation than that observed after resistant mice infection by the same route. Subcutaneous air-pouch inoculation of *P. brasiliensis* elicited a controlled and limited infection that produced a PMN-rich exudate, thus favoring the study of the interaction between the fungus and the neutrophils. Susceptible mice produced higher numbers of PMN; however, these cells were less effective in killing the fungi. Inflammatory cytokines were more pronounced in resistant mice, which supports their PCM raised resistance.

1. Introduction

Paracoccidioidomycosis (PCM) is, out of several other fungal infections, an important and neglected systemic condition that can be easily found in Latin America and especially in Brazil [1]. PCM leads to lung, mucosal, and skin involvement that may comprise acute and even chronic presentation of the disease [2, 3]. Actually, the primary acute PCM infection is later transformed to a chronic phase and its severity depends essentially on the host's immune response [4].

Flaws in immune cell activation and also immune suppression lead to a higher susceptibility to PCM [5, 6]. Accordingly, several inflammatory cells and exceptionally the neutrophils (PMN) are crucial to build the host's response against PCM's fungal agent *Paracoccidioides brasiliensis (Pb)* [7]; such response involves the release and production of antimicrobial factors, cytokines, chemokines, serum antibodies, and so forth [2, 8].

In that way, PMN are mainly constituents of the innate immune response but can also trigger and modulate adaptive