

Infections associated with chronic granulomatous disease- Is there genetic linkage between the genotype to the phenotypic expression of the disease? New insights on diagnosis, management and prevention of infections

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CGD is an inherited primary immunodeficiency characterized by the absence or malfunction of the nicotinamide dinucleotide phosphate (NADPH) oxidase in phagocytic cells. As a result, there is an impaired ability to generate superoxide anion and the subsequent reactive oxygen intermediates (ROI). Consequently, CGD patients suffer from two clinical manifestations: recurrent, life-threatening bacterial and fungal infections and excessive inflammatory reactions leading to granulomatous lesions. Although the genotype of CGD was linked to the phenotypic expression of the disease, this connection is still controversial and poorly understood. Certain correlations were reported, but the clinical expression of the disease is usually unpredictable, regardless the pattern of inheritance.

CGD mainly affects lungs, lymph nodes, skin, gastrointestinal tract and liver. Patients are particularly susceptible to catalase-positive micro-organisms, including *Staphylococcus aureus*, *Nocardia spp.* and *Gram-negative bacteria*, as *Serratia marcescens*, *Burkholderia cepacea* and *Salmonella spp.* Unusually, catalase negative microorganisms were reported as well. New anti-bacterial and anti-mycotic agents considerable improved the prognosis of CGD. Prevention of infections changed significantly the survival of CGD patients. The therapy with interferon γ is still controversial. Bone marrow stem cell transplantation is currently the curative treatment. Gene therapy needs further development. In this review we discuss genetic, functional and molecular aspects of CGD and their impact on the clinical expression, infectious complications and the hyperinflammatory state.

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