Mycobacterial disease in patients with chronic granulomatous disease: A retrospective analysis of 71 cases

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Paris and Saint Denis Reunion, France; Rome, Italy; Mexico City, Tlalpan, and Merida, Mexico; Beijing, China; Izmir, Konya, Ankara, and Istanbul, Turkey; São Paulo and Curitiba, Brazil; Casablanca, Morocco; La Plata, Buenos Aires, and Rosario, Argentina; San Salvador, El Salvador; Beirut, Lebanon; Sousse and Tunis-Belvèdère, Tunisia; Bogota, Columbia; Concepción, Chile; Abu Dhabi, United Arab Emirates; Algiers, Algeria; Riyadh, Saudi Arabia; Kiev, Ukraine; Bratislava, Slovakia; New York, NY; and Tehran, Iran

Background: Chronic granulomatous disease (CGD) is a rare primary immunodeficiency caused by inborn errors of the phagocyte nicotinamide adenine dinucleotide phosphate oxidase complex. From the first year of life onward, most affected patients display multiple, severe, and recurrent infections caused by bacteria and fungi. Mycobacterial infections have also been reported in some patients.

Objective: Our objective was to assess the effect of mycobacterial disease in patients with CGD.

Methods: We analyzed retrospectively the clinical features of mycobacterial disease in 71 patients with CGD. Tuberculosis and BCG disease were diagnosed on the basis of microbiological, pathological, and/or clinical criteria.

Results: Thirty-one (44%) patients had tuberculosis, and 53 (75%) presented with adverse effects of BCG vaccination; 13 (18%) had both tuberculosis and BCG infections. None of these patients displayed clinical disease caused by environmental mycobacteria, *Mycobacterium leprae*, or *Mycobacterium ulcerans*. Most patients (76%) also had other pyogenic and fungal infections, but 24% presented solely with mycobacterial disease. Most patients presented a single localized episode of mycobacterial disease (37%), but recurrence (18%), disseminated disease (27%), and even death (18%) were also observed. One common feature in these patients was an early age at presentation for BCG disease. Mycobacterial disease was the first clinical manifestation of CGD in 60% of these patients.

Conclusion: Mycobacterial disease is relatively common in patients with CGD living in countries in which tuberculosis is endemic, BCG vaccine is mandatory, or both. Adverse reactions to BCG and severe forms of tuberculosis should lead to a suspicion of CGD. BCG vaccine is contraindicated in patients with CGD. (J Allergy Clin Immunol 2016;■■■:■■■-■■■.)

Key words: *Mycobacteria, BCG, chronic granulomatous disease, tuberculosis, primary immunodeficiency*

Chronic granulomatous disease (CGD) is a primary immunodeficiency (PID) characterized by the production of reactive oxygen species in small amounts, if at all, by phagocytes because of a deficiency of nicotinamide adenine dinucleotide phosphate (NADPH) oxidase.[1-3] The phagocyte NADPH oxidase is an enzymatic complex composed of a membrane-bound core, the heterodimeric flavocytochrome, consisting of gp91^{phox} (encoded by *CYBB*) and p22^{phox} *(CYBA)*, and the cytosolic subunits p47^{phox} *(NCF1)*, p67^{phox} *(NCF2)*, and p40^{phox} *(NCF4)*. Mutations in any of the 5 genes (*CYBB*, *CYBA*, *NCF1*, *NCF2*, and *NCF4*) encoding the membrane-bound or cytosolic components of the phagocyte NADPH oxidase are responsible for CGD.[4-7]

Affected patients experience severe and recurrent infections caused by a diverse but relatively specific set of bacteria and fungi and from uncontrolled inflammation that can lead to granuloma