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Sarcoidosis in coexistence with chronic granulomatous disease

Abstract

Granulomas formations are present in many lung diseases. Coexistence of one or more of these diseases is very rare. Diagnostics of such cases always poses a challenge. We present a case of coexistence of chronic granulomatous disease (CGD) and sarcoidosis.

Key words: chronic granulomatous disease, sarcoidosis, granulomas

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Introduction

Chronic granulomatous disease (CGD) is a rare inherited primary immunodeficiency disorder. There are two inheritance patterns of CGD: an autosomal recessive manner and the X-linked manner. Mutations in the *CYBB*, *CYBA*, *NCF1*, *NCF2* and *NCF4* genes are responsible for inappropriate function of structural or regulatory subunits of phagocyte nicotinamide adenine dinucleotide phosphate (NADPH) oxidase [1]. These genetic defects are presented with an impaired respiratory burst in phagocytes (neutrophils, mononuclear cells, macrophages, and eosinophils). Absence or minimal (low) respiratory burst activity, that is crucial for generating superoxide, the precursor of hydrogen peroxide and other reactive oxygen intermediates (ROI), leads to recurrent bacterial and fungal infections [1, 2]. Every organ or tissue may be affected, but the skin, lungs, lymph nodes, liver and bones are the most frequent sites of infection. Granulomas formations in multiple organs are the second characteristic feature of CGD [1, 3].

Granulomas are areas of macrophages which are transformed into epithelial-like cells called histiocytes or epithelioid cells, admixed with other inflammatory cells such as lymphocytes and plasma cells [4–6]. Etiology of granulomas divides them into two histologic subtypes: foreign-body giant cell granulomas and immune granulomas [6]. The last group further splits into necrotizing and non-necrotizing granulomas.

Granulomatous disorders are numerous and include infections, vasculitis, immunological upsets, leukocyte oxidase defects, hypersensitivity, exposure to chemicals, and neoplasia [5]. The most common noninfectious condition where granulomas are found is sarcoidosis [5, 7, 8]

The following report describes a rare case of coexistence of both CGD and sarcoidosis.

Case report

A 28-year-old non-smoking man known to be suffering from CGD was admitted to our hospital in order to investigate persistent, unproductive cough and shortness of breath. In childhood he had been hospitalized multiple times in pediatric departments, presenting recurrent fever, lymphadenopathy, infections of the lower respiratory tract and liver abscesses. Initial laboratory tests had revealed microcytic anemia, anisocytosis, leukocytosis, very high marker of inflammation, hypergammaglobulinemia. CGD had been properly diagnosed at the age of 13 in immunology

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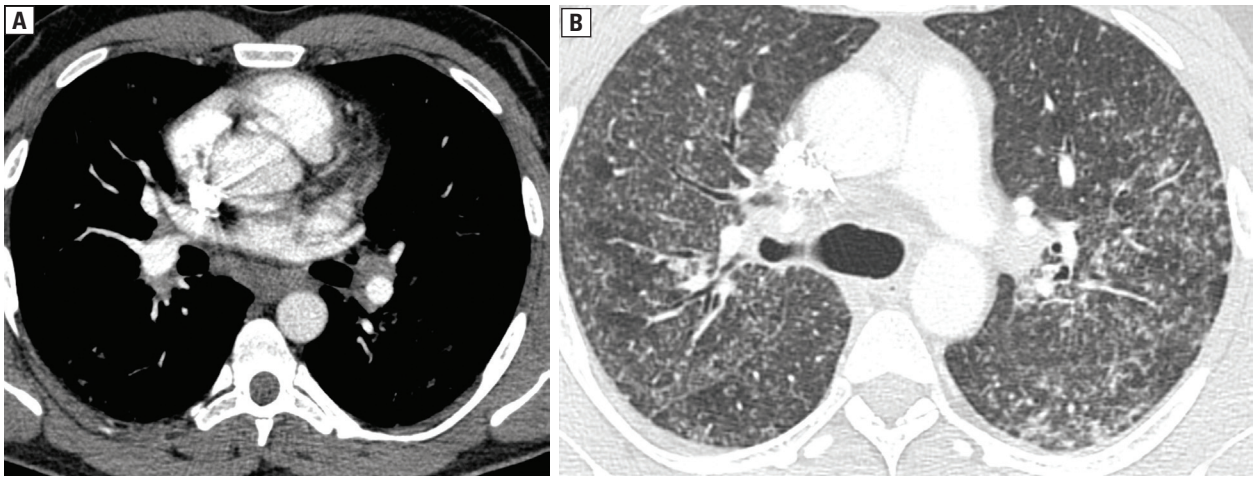

Figure 1A. Contrast enhanced computed tomography (CT) scan, mediastinal window, at the level of hila, depicts hilar and subcarinal lymph nodes enlargement; **B.** High-resolution CT (HRCT) scan at the level of trachea demonstrates multiple small nodules in upper lobes in peribronchiolar location, mainly subpleural and perifissural

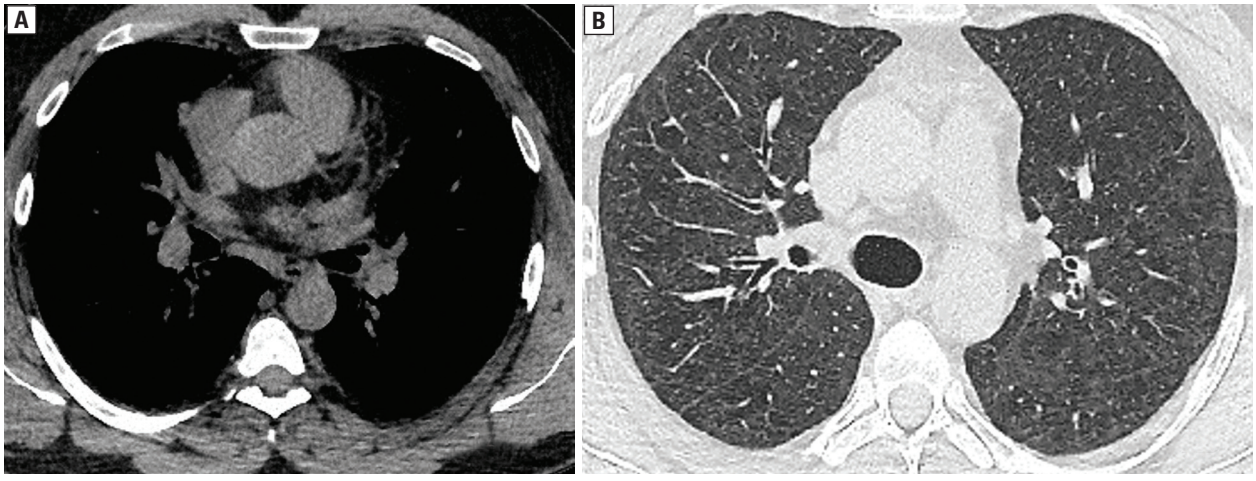

Figure 2A. Contrast non-enhanced CT scan, mediastinal window, depicts regression of mediastinal and hilar adenopathy; **B.** HRCT scan shows partial regression of nodules

department and received prescribed antibacterial (trimethoprim/sufamethoxazole 5 mg/kg/day) and antifungal prophylaxis (firstly itraconazole 5 mg/kg/day then posaconazole 600 mg daily) longitudinally. At the time of admission the patient complained about left shoulder joint pain accompanied with erythema nodosum in the past. On physical examination, there were no abnormalities. Chest X-ray showed bilateral hilar lymphadenopathy with nodular opacities distributed especially in middle zone, that was absent in his previous radiograms (Figures 1A, B). Chest computed tomography (CT) showed bilateral hilar and mediastinal lymphadenopathy as well as widespread nodules present especially along interlobular septa and subpleurally. Fiberoptic bronchoscopy showed normal bronchial tree. Endobronchial ultrasound-guided lymph node biopsy and bronchoscopic lung cryobiopsy were performed. Histological examination revealed non-necrotising granulomata consistent with sarcoidosis. The culture of endobronchial samples was negative for M. tuberculosis, other bacteria and fungi. Pulmonary function tests revealed a restrictive pattern (TLC 76% pred, FVC 59% pred, FEV_1 62% pred.) with no significant post-bronchodilator improvement and reduced transfer factor for carbon monoxide (TL_{CO}) to 48% pred. The 6 min. walk distance (6MWD) was 590 m, with oxygen desaturation from 97% to 84%.

In February 2016, due to lung functional impairment caused by sarcoidosis, prednisone treatment at 0.5 mg/kg/day was started. This treatment

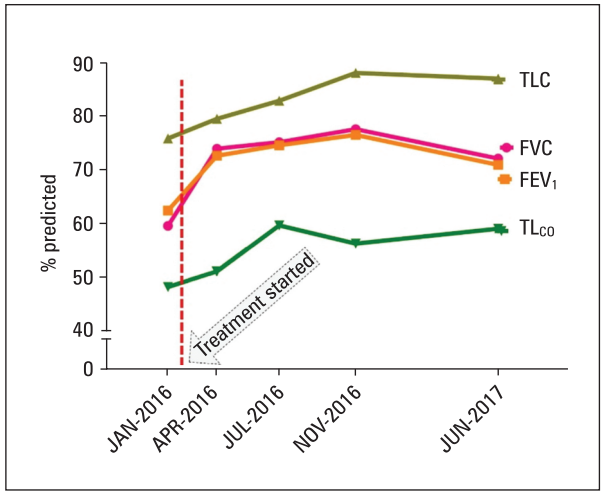

Figure 3. Lung function indices expressed as % of predicted before and during the treatment TLC — total lung capacity; FEV_1 — forced expiratory volume at first second; FVC — forced vital capacity; TL_{CO} — single breath carbon monoxide transfer factor of the lung

was effective and already after 2 months, clinical, radiographic (Figures 2A, B) and functional improvement (Figure 3) were observed.

Based on clinical, radiological and histopathological findings with exclusion of the other reasons of such test results and very good response to corticosteroids treatment, the diagnosis of sarcoidosis was confirmed.

Discussion

There have only been few cases reported where sarcoidosis and CGD coexisted [8]. The incidence of CGD is about 1 per 200 000 live births whereas sarcoidosis affects 1 to 50 per 100 000 individuals and is the most common cause of lung granulomas unrelated to infection [8]. The real number of cases with coexistence of both diseases is unknown. Due to lack of defined criteria of sarcoidosis it is very often a diagnosis of exclusion. Granulomas however accompany a wide variety of other diseases. These disorders are commonly divided into two groups with infectious and noninfectious background. The first group refers to mycobacterial tuberculosis and non — tuberculous mycobacterial infections as well as fungal or parasite infections [4, 8]. Noninfectious causes of lung granulomas include numerous conditions which comprise, aside from sarcoidosis, other interstitial lung diseases, antinuclear antibody associated diseases, immunodeficiency disorders, lymphoproliferative disorders, connective tissue diseases and granulomas related to foreign bodies [8]. Considering some of these conditions may coexist, as is often the case, the differential diagnosis can be challenging. Maintaining an acute clinical awareness of this coexistence minimizes the risk of misdiagnosis or delayed diagnosis and leads to early and appropriate treatment allowing a reduction of long term complications.

Conflict of interest

None declared.

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