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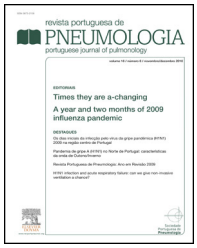

CASE REPORT

Chronic granulomatous disease associated with common variable immunodeficiency – 2 clinical cases

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KEYWORDS
Common variable immunodeficiency;
Granulomas;
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Abstract
Introduction: Chronic granulomatous disease associated with common variable immunodeficiency (GD-CVID), although well documented, is rare. Granulomatous lesions can affect several organs and are histologically indistinguishable from sarcoidosis.
Clinical cases: Case 1: A 39-year-old male patient with CVID, asymptomatic although with thrombocytopenia and mediastinal-hilar adenopathies. GD-CVID was diagnosed by bone marrow biopsy. Progressive clinical and radiological improvement was obtained with corticotherapy.
Case 2: A 38-year-old male patient with CVID, suffered from asthenia, anorexia, myalgia, lower limbs edemas, and dry cough. He had mediastinal and bilateral hilar adenopathies within which biopsy revealed non-necrotizing granulomatous infiltrate. A spontaneous resolution was detected after 9 months of evolution.
Conclusion: GD-CVID is rare and can mimetize other pathologies, namely, sarcoidosis; it should therefore be publicized and discussed so that it becomes a general clinical knowledge.

PALAVRAS-CHAVE
Imunodeficiência comum variável;
Granulomas;
Sarcoidose;
Doença granulomatosa

Doença granulomatosa crónica associada com a imunodeficiência comum variável - 2 casos clínicos

Resumo
Introdução: A doença granulomatosa crónica associada à imunodeficiência comum variável (DG-IDCV), apesar de bem documentada, é rara. As lesões granulomatosas podem afectar vários orgãos e são histologicamente indistinguíveis daquelas que caracterizam a sarcoidose.
Casos clínicos: Caso 1: Doente do sexo masculino, 39 anos, com diagnóstico de imunodeficiência comum variável, clinicamente assintomático, com trombocitopenia e adenopatias pré-traqueais e hilares de novo. O diagnóstico de DG-IDCV foi obtido por biópsia de medula óssea. Iniciou tratamento com corticoterapia com melhoria clínica e radiológica progressiva.

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Caso 2: Doente do sexo masculino, 38 anos, com diagnóstico de imunodeficiência comum variável, com queixas de astenia, anorexia, mialgias, edemas dos membros inferiores e tosse seca. Adenopatias mediastínicas e hilares bilaterais cuja biopsia revelou infiltrado granulomatoso não necrotizante. Observou-se uma resolução espontânea após nove meses de evolução.
Conclusão: A doença granulomatosa crónica associada a imunodeficiência comum variável é rara. Dado que esta entidade pode mimetizar outras patologias, nomeadamente a sarcoidose, os casos clínicos que se referem à mesma devem ser publicados e discutidos para conhecimento clínico geral.

Introduction

Common variable immunodeficiency (CVID) is a rare primary immunodeficiency syndrome characterized by impaired B-cell differentiation with inaccurate immunoglobulin production.[1] It is defined by markedly reduced serum concentrations of IgG, combined with low levels of IgA and/or IgM, poor or absent response to immunizations in a patient without any other signs of immunodeficiency. The prevalence in Europe is estimated to be around 1:50,000–1:200,000.[2] The etiology is still unknown, but it appears to result from a variety of gene defects (e.g., ICOS, TACI, BAFF-R, CD19, CD20, CD21, and CD81), most of which are sporadic rather than familiar.[2–4]

Although rare, systemic granulomatous disease related to CVID is well documented (>50 case reports). Granulomatous non-caseous lesions can be detected in the lung, liver, spleen, gastrointestinal tract, lymph nodes, skin and eye in almost 10% of the patients with CVID.[2,5] Some of them also show clinical manifestations similar to sarcoidosis, with symptoms like dyspnea, persistent cough, asthenia, anorexia and arthralgia.[6,7] Granulomatous lesions in CVID may not only affect the same organs as sarcoidosis but also be histologically indistinguishable.[8–11] As a consequence, sarcoidosis is often incorrectly diagnosed in GD-CVID patients, with GD-CVID considered as a distinguished entity.[12–15]

The authors present two clinical cases of CVID with systemic involvement by non- caseous granulomas.

Clinical cases

1st case

A 39-year-old male, mechanic engineer, non-smoker, had been diagnosed with CVID 4 years ago, under treatment with intravenous IgG. He had previously had several respiratory infections since childhood. In November 2009, after a routine chest X-ray with mediastinum enlargement, a thoracic CT scan was performed and numerous adenopathies in the prevascular, pretracheal as well as in the right pulmonary hilum were observed. Additionally, diffuse peribronchovascular micronodules were detected in lung parenchyma (Fig. 1 and 2). The patient had no relevant clinical complaints or alterations at physical examination. Besides hypogammaglobulinemia (IgG 287 mg/dL; IgM 8 mg/dL; IgA 6 mg/dL) and slight thrombocytopenia (platelets 127×10^3 μL), no other serum related alterations were noticed. Lung function tests revealed a mild obstructive pattern. A bronchoscopy with bronchoalveolar lavage (BAL) was performed. It showed lymphocytic alveolitis (28%) with a slight increase in CD4/CD8 ratio (2.2), and no microorganism was isolated or malignant cell detected. A bone marrow biopsy was also performed, which showed non-caseous granulomas. There were no clinical or imagiological indications of other organ involvement. At this stage, the patient was started on oral corticotherapy which led to progressive clinical and radiological improvement ending in total disease resolution which continued after the patient come off medication.

2nd case

A 38-year-old male nurse, a non-smoker, had been diagnosed with CVID a year earlier, treated with intravenous IgG. Previously, he had had several respiratory infections since childhood. In February 2010, he began to suffer from asthenia, anorexia, and erythema nodosum. A thoracic CT scan showed mediastinal and bilateral symmetrical hilar adenopathies. Lung function tests were normal. Bronchoscopy with BAL revealed lymphocytosis (35%) with a slight increase in CD4/CD8 ratio (2.6) and no microorganism or malignant cells were detected. Endobronchial ultrasound biopsy showed non-necrotizing granulomatous infiltration. There were no signs of extrathoracic involvement. After diagnosis, he was prescribed symptomatic therapy only (antitussives and anti-inflammatories). After 6 months, there was a spontaneous resolution of the disease, that is to say, the patient became asymptomatic and no imagiologic alterations or signs of recurrence have been detected so far.

Discussion

CVID is a heterogeneous disease, characterized by recurrent infections, particularly bacterial infections often occurring in the respiratory or gastrointestinal tract, autoimmunity phenomena, predisposition to malignant diseases, and