

PULMONARY PARACOCCIDIOIDOMYCOSIS AND REVERSED HALO SIGN: A TWO-CASE REPORT*

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Abstract The present study reports two histologically proven cases of pulmonary paracoccidioidomycosis where a reversed halo sign was found. The reversed halo, initially described as a pathognomonic sign of cryptogenic organizing pneumonia, has later been found and described in paracoccidioidomycosis.

Keywords: Reversed halo sign; Paracoccidioidomycosis; Cryptogenic organizing pneumonia.

Resumo *Paracoccidioidomicose pulmonar: relato de dois casos enfatizando o sinal do halo invertido.* Este trabalho relata dois casos de paracoccidioidomicose pulmonar comprovados histologicamente, nos quais foi encontrado o sinal radiológico do halo invertido. Este sinal, descrito inicialmente como patognomônico da pneumonia criptogênica em organização, foi posteriormente encontrado e descrito na paracoccidioidomicose.

Unitermos: Halo invertido; Paracoccidioidomicose; Pneumonia criptogênica em organização.

INTRODUCTION

Paracoccidioidomycosis is the most prevalent systemic fungal infection in Latin America, particularly in Brazil⁽¹⁾. This disease is caused by the single dimorphic species *Paracoccidioides brasiliensis* and is the most significant type of mycosis in our environment. As a deep mycosis, it is not limited to the epithelial surface of the organism, invading conjunctive tissue and viscera⁽²⁾. Pulmonary, cutaneous, mucosal are the predominant clinical presentations of this disease. Lungs are affected in approximately 75% of cases⁽²⁾, and in 10% of these cases the reversed halo sign may be found on high-resolution computed tomography (HRCT)⁽³⁾.

CASES REPORT

Case 1

A male, 37-year-old peasant living in Mato Grosso do Sul and presenting with progressive dyspnea for one week, has been referred to the service to be submitted to chest computed tomography (CT).

Chest radiography had demonstrated bilateral reticulonodular opacity, predominantly in the upper thirds, with consolidation in the middle third of the left pulmonary field.

The patient presented in a good general condition, eupneic, ruddy, and afebrile, complaining of odynophagia and pain in the mesogastrium. He denied thoracic pain and cough. At physical examination, painful, bilateral submandibular lymph nodes enlargement (measuring about 1.0 cm) was found attached to the deep planes, with absent trophic alterations of the adjacent skin. The soft palate presented a granulomatous hyperemic lesion. Bilateral, ulcerative lesions were found on the jugal mucosa. Unaltered cardiopulmonary symptomatology, and painful abdomen under hypogastric palpation.

Chest HRCT showed diffuse nodular opacities, cavitated images, consolidation, ground-glass attenuation and subpleural reversed halo sign. The patient has also been submitted to abdominal ultrasonography and spirometry that have demonstrated no alteration.

Incisional biopsy of granulomatous le-

sion of the mouth revealed squamous epithelial hyperplasia, intraepithelial microabscesses and granulomatous reaction with epithelial histiocytes, multinucleated giant cells, and central accumulation of polymorphonuclear neutrophils. Elongated and round fungi with thick and refractive capsules were observed inside the giant cells. The histopathological diagnosis was paracoccidioidomycosis.

The patient has been medicated with itraconazol (200 mg/ day), and was discharged with no complaint, after improvement of the pulmonary condition. He has been under clinical follow-up for two months, and using prophylactic suphame-toxazole + trimethoprim.

Case 2

A male, thirty-nine-year old peasant, born in Guairá, SP, Brazil, has been referred to the service to be submitted to chest radiography because of a productive cough, hemoptysis and progressive dyspnea that had initiated for one month and a half.

The patient presented in a good general condition, with a history of irregular fever, lesions in the oral cavity and 10 kg weight loss. At clinical examination, a granulomatous lesion was observed on the right lip commissure involving jugal mucosa and gingiva, besides a limited opening of the mouth. At pulmonary auscultation, a vesicular murmur was observed, with bron-

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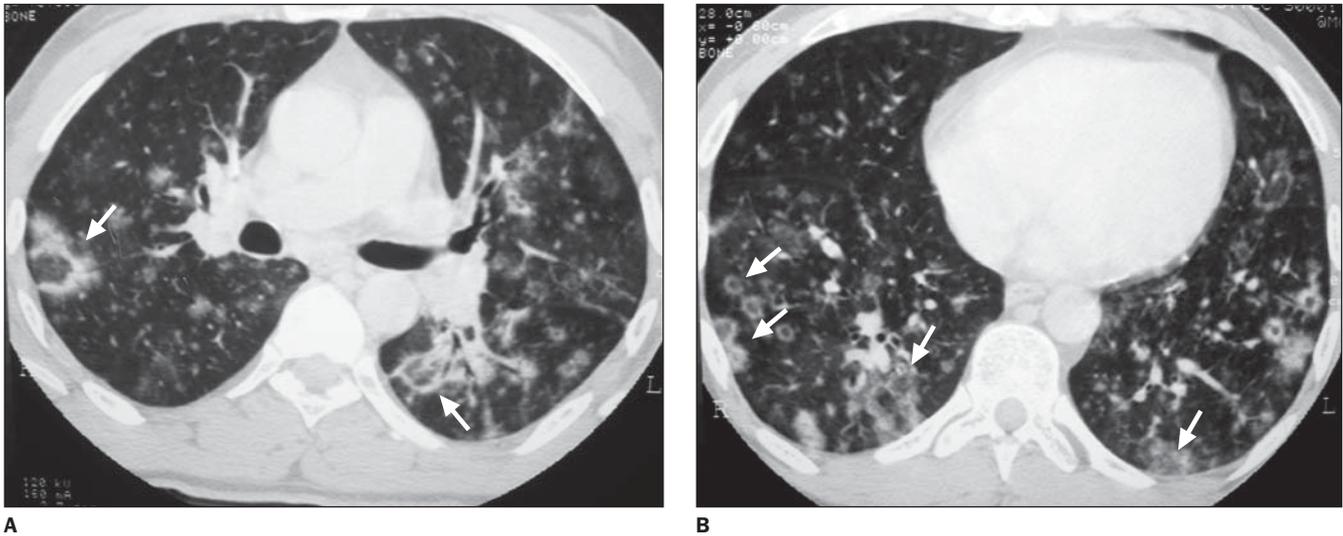


Figure 1. Case 1. HRCT showing reversed halo sign (arrows). Besides small, sparse cavitated nodules.

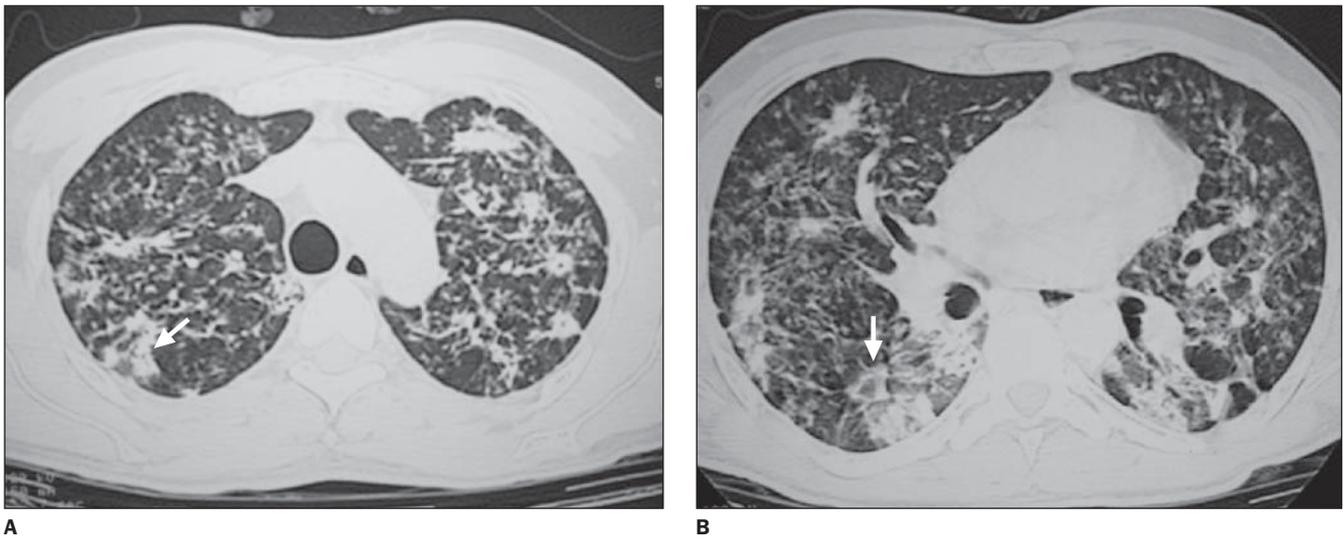


Figure 2. Case 2. HRCT showing reversed halo sign (arrows), besides interlobular septal thickening and thick-walled cavitated nodules.

chophony over the middle third of the left lung, and hyperresonance under auscultatory percussion. Cardiac and abdominal symptomatology with no clinical evidence. Absence of palpable enlarged lymph nodes.

Plain chest radiograph has demonstrated diffuse and bilateral gross, reticulonodular opacities with sparse foci of consolidation on the lower and middle pulmonary fields. HRCT has demonstrated significant architectural distortion, extensive foci of subpleural consolidation, nodular cavitation, interlobular septal thickening, parenchymal bands, sparse foci of ground-glass attenuation, air-space nodular opaci-

ties and some areas with reversed halo sign in lower lobes.

Bronchoscopy has demonstrated the presence of hyaline secretion in the whole bronchial tree, a pale mucosa with signs of bronchitis, and increased diameter of bronchial segments. Endobronchial washing, brushing and biopsy were performed. Bronchial brushing has demonstrated the presence of columnar cells, large amount of neutrophils, eosinophils and numerous histiocytes, with presence of multinuclear, giant cells, including round structures with birefractive membrane compatible with *P. brasiliensis*. The typical resemblance of the

fungus to a ship's steering wheel was found. Malignancy has not been found. Negative test for alcohol-acid resistant bacilli in the bronchial washing and negative tuberculosis test. Biopsy of the granulomatous lesion on the oral mucosa has diagnosed paracoccidioidomycosis.

The patient has been medicated with itraconazol and sulphametoxazole + trimethoprim, with an excellent clinical progress.

DISCUSSION

Paracoccidioidomycosis predominantly affects young men and peasants living in

rural zones. The disease is acquired by inhalation of infectious particles of the fungus *P. brasiliensis* involving lungs, upper respiratory and digestive mucosas, central nervous system, suprarenal glands and lymph nodes⁽⁴⁾.

Main clinical presentations include fever, cough, weight loss, hemoptysis, odynophagia, lymph node enlargement, ulcerative or granulomatous lesions on the upper digestive and respiratory mucosas.

Radiological pulmonary findings include interlobular septal thickening, nodular opacities, thickening of the peribronchovascular interstice, intralobular lines, ground-glass attenuation, cavitations, air-space consolidation, traction bronchiectasis, irregular increase of the air-space^(2,5) and reversed halo sign⁽³⁾.

The reversed halo sign is defined as a focal round area of ground-glass attenuation and surrounding air-space consolidation of crescent (forming more than three quarters of a circle) or ring (a complete circle) shapes^(3,6). Histologically, central ground-glass attenuation corresponds to an inflammatory infiltrate in the alveolar septum with macrophages, lymphocytes, plasmatic cells and some giant cells with a relative preservation of alveolar spaces. Peripheral consolidation consists of a dense and homogeneous, intra-alveolar cellular infiltrate. Evidence of organizing pneumonia is not found. Presence of *P. brasiliensis* is observed inside alveolar septa and air-spaces. These findings indicate that the reversed halo sign may be found in indi-

viduals affected by active infection by *P. brasiliensis*⁽³⁾.

Central ground-glass attenuation surrounded by dense consolidation of crescent or ring shapes as a finding of HRCT was reported in 1996 by Voloudaki et al.⁽⁷⁾ in patients affected by cryptogenic organizing pneumonia. Histological studies have demonstrated that ground-glass attenuation corresponded to alveolar septal inflammation and cellular debris, and peripheral opacity of crescent or ring shapes, to consolidation and areas of organizing pneumonia inside alveolar ducts⁽³⁾.

In 2003, Kim et al.⁽⁶⁾ reviewed patients affected by cryptogenic organizing pneumonias with HRCT findings of focal ground-glass attenuation surrounded by consolidation of crescent and ring shapes with the same histological characteristics described by Voloudaki et al.⁽⁷⁾, and called this finding "reversed halo sign"⁽⁶⁾.

Recently, Gasparetto et al.⁽³⁾ described the association between reversed halo sign and paracoccidioidomycosis. In a study of 148 patients diagnosed with paracoccidioidomycosis, 15 presented with this finding. In two cases, the reversed halo sign was the only finding on HRCT. Three patients presented only one image of reversed halo sign, one had two lesions, and the others presented with multiple lesions. The prevalent sites of presentation were middle and lower pulmonary fields. Also, the reversed halo sign was predominantly found in peripheral zones, with diameters ranging between 10 and 50 mm (mean 20 mm)⁽³⁾.

CONCLUSION

Recent studies suggest that active paracoccidioidomycosis may course with reversed halo sign. About 10% of patients with active infection by *P. brasiliensis* may present with this finding that is not specific of cryptogenic organizing pneumonia.

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