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Pulmonary adiaspiromycosis: report of two cases

Adiaspiromicose pulmonar: relato de dois casos

Vitorino Modesto dos Santos[1 4], Marcelo Cunha Fatureto[2], João Carlos Saldanha[3] and Sheila Jorge Adad[3 4]

Abstract *Two cases of human pulmonary adiaspiromycosis are reported. Patients were 29 and 54-year-old males, farm workers, with "grippe-like" symptoms and radiographic findings suggestive of granulomatous interstitial disease. Transthoracoscopic and transbronchial biopsies were performed. Pulmonary function was measured by spirometry. One patient used ketoconazole. Possibility of misdiagnosed pulmonary adiaspiromycosis is emphasized.*

Key-words: *Pulmonary mycosis. Adiaspiromycosis.* Emmonsia parva *var* crescens. Chrysosporium parvum *var* crescens*. Pulmonary biopsy. Spirometry.*

Resumo *Relatam-se casos de adiaspiromicose pulmonar em homens brancos de 29 e 54 anos, lavradores, com sintomas "gripais" e achados radiológicos sugestivos de doença granulomatosa intersticial. Biópsias transbrônquicas e transtoracoscópicas foram realizadas. A função pulmonar foi avaliada por espirometria. Um paciente usou cetoconazol. Enfatizam-se possibilidades de confusão diagnóstica na adiaspiromicose pulmonar.*

Palavras-chaves: *Micoses pulmonares. Adiaspiromicose.* Emmonsia parva *var* crescens. Chrysosporium parvum *var* crescens*. Biópsia pulmonar. Espirometria.*

Adiaspiromycosis is a rare pulmonary disease described in humans. It is a common fungal infection of lower order mammals, most usually wild rodents, with wide geographical distribution. This disease is caused by a geophilic fungus, *Emmonsia parva* var *crescens*[14 18], whose dust-borne mycelial phase (conidia) may be accidentally inhaled and produce a perifocal granulomatous inflammatory reaction in the lungs[14]. In immunocompetent patients, fungus dissemination to extra pulmonary sites has not been reported[8 10 11 17 19]. Adiaconidia are spherical and do not replicate, but million fold increase in volume (diameter from 2.5 to 700mm)[2 9 20], compress pulmonary parenchyma inducing an intense inflammatory reaction, and soon degenerate and die[18]. Severity of lung lesions, clinical manifestations and pulmonary function changes will depend on the amount and distribution of inhaled conidia[20 27], associated diseases, fungus antigenicity[1] and host immune response. The disease may be cured without treatment[18], even the disseminated pulmonary form, which sometimes causes death[19 21].

We report two cases of this unusual deep mycosis that would correspond to the 19th and 20th cases described in Brazil[18]. Similar to our previous report[24], these cases were also diagnosed through transthoracoscopic lung biopsies performed at hospitals in Uberaba, MG.

1. Departamento de Clínica Médica. 2. Disciplina de Cirurgia Torácica; 3. Disciplina de Patologia Especial; 4. Curso de Pós-graduação em Patologia da Faculdade de Medicina do Triângulo Mineiro (FMTM), Uberaba, MG.
Financial support: Fundação de Ensino e Pesquisa de Uberaba (FUNEPU).
Endereço para correspondência: Prof. Marcelo Cunha Fatureto. Disciplina de Cirurgia Torácica. Hospital Escola/FMTM. Av. Getúlio Guaritá s/n, 38057-020 Uberaba, MG.
e-mail: mfat@zaz.com.br
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CASE REPORTS

Case 1. EB, a 54-year-old white male farm worker, natural from Arapuá, MG. Cigarette smoker (pack year: 25). Before admission, a chest x-ray film showed micronodular interstitial infiltration in both lungs (Figure 1) and for suspicious pneumonia he had used penicillin and gentamicin without any clinical or radiological improvement. On admission (09/27/97), he presented fever (38ºC), headache, myalgia, nausea and weight loss. Physical examination was otherwise normal. The routine laboratory tests were normal, except for leukocytosis (13,500/mm^3) and neutrophilia (86%). Spirometry showed severe restrictive disturbance, with forced vital capacity (FVC): 1,490ml (39.6%, predicted: 3,760ml)[26]. Thorax computerized tomography (CT) revealed a diffuse interstitial micronodular infiltrate and septal lines suggestive of mycosis (Figure 1). Fiberoptic bronchoscopy was normal and neither mycobacteria nor fungus

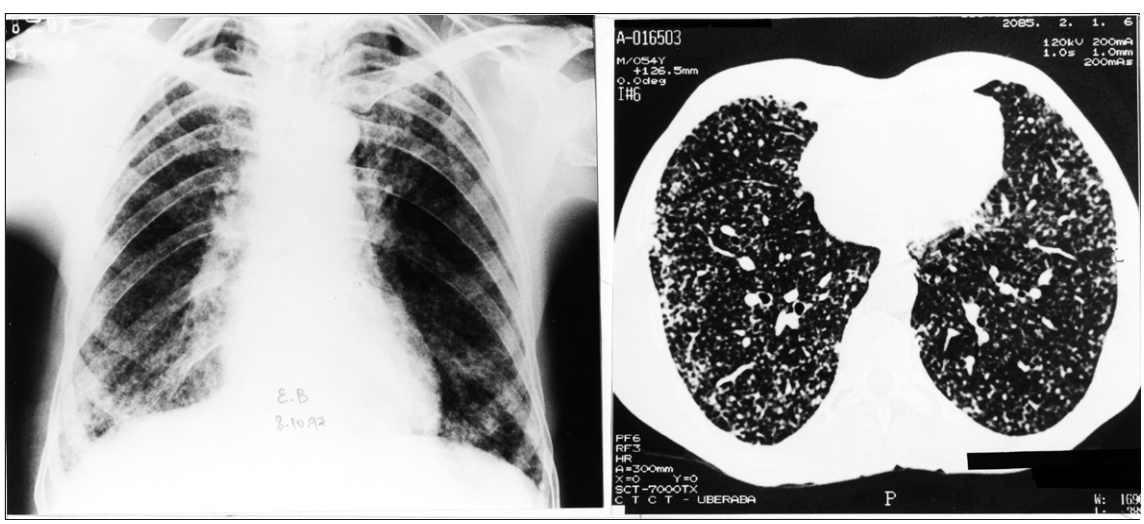

Figure 1 – Case 1 chest x-ray and CT, showing diffuse and bilateral micronodular interstitial and linear septal infiltrate.

were present in samples of the bronchoalveolar lavage aspirate or in the transbronchial biopsy material. On video assisted lung biopsy, the pleural surface appearance was normal; nevertheless, the histopathological study revealed pulmonary adiaspiromycosis. Microscopically, there was an intense chronic inflammatory reaction in the alveolar tissue, with mixed granulomas development. Granulomas were characterized by a lymphocytic and plasmacytic infiltrate surrounded by a palisade of histiocytes, and in whose center pathogenic microorganisms involved by neutrophils were observed (Figure 2). In some granulomas there was a necrotic center with abundant polimorphonuclear neutrophils, without evidence of the fungus. Adiaconidia were easily identified through their round or ovoid large size, the densely silver staining thick wall and the granular complex inner structure.

Patient used ketoconazole (200mg/day) during two months and, on 11/20/97 he was symptomless. Spirometry showed mild restrictive disturbance, with FVC: 2,520ml (67%, predicted: 3,760ml)[26]. In 02/05/98, spirometry was normal, with FVC: 3,230ml (85.9%, predicted: 3,760ml)[26]. In 06/18/98, he had no complaints, with body mass index: 20.78kg/m^2, normal blood counts and normal spirometry results. Comparatively, the chest x-ray and CT films showed less intense granular interstitial infiltrate and interlobular septal lines (Figure 3).

Case 2. HPC, a 29-year-old white male farm worker, natural from São Gotardo, MG. Cigarette smoker (pack year: 18). Before admission, a chest x-ray film showed bilateral miliary pulmonary

infiltration and he had received rifampin 600mg/day, isoniazid 400mg/day and pyrazinamide 2g/day. On admission (12/22/97), he was complaining of fever (38.5° C), dry cough, right anterior pleural pain, breathlessness with exercise and weight loss. Physical examination disclosed mild anemia, respiratory rate 36/min, dry rales and wheezing in both lungs. Except for leukocytosis (12,300/mm^3)

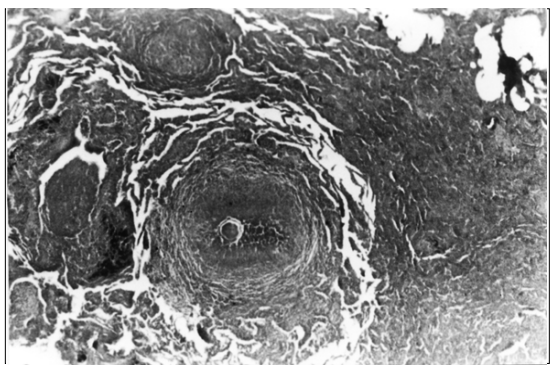

Figure 2 – Case 1 photomicrography showing mixed granulomas, the largest containing a central adiaconidium, surrounded by polymorphonuclear neutrophils, a palisade of macrophages and a lymphocytic and plasmacytic halo. Some granulomas without evidence of adiaconidia are observed. (HE, 40X).

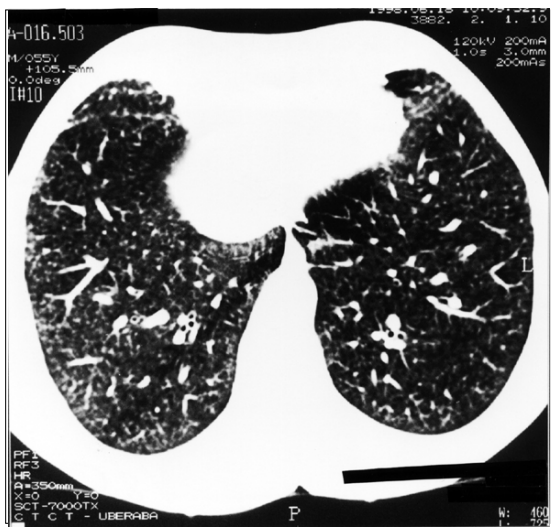

Figure 3 – Case 1 control chest CT revealing regression of the interstitial and septal infiltrate.

and neutrophilia (82%), routine laboratory tests were normal. Chest x-ray films showed bilateral diffuse interstitial micronodular infiltrate (Figure 4).

Fiberoptic bronchoscopy was normal. The middle lobe transbronchial biopsy revealed granulomas containing epithelioid histiocytes surrounded by lymphocytes, rare eosinophils and fibrosis. Centrally located in a granuloma, there was a periodic acid Schiff (PAS) positive spherical structure with a trilaminar wall, containing a granular eosinophilic material, morphologically compatible with the diagnosis of pulmonary adiaspiromycosis (Figure 5). The transthoracoscopic pulmonary biopsy showed a round structure limited by two walls, the outer deeply eosinophilic

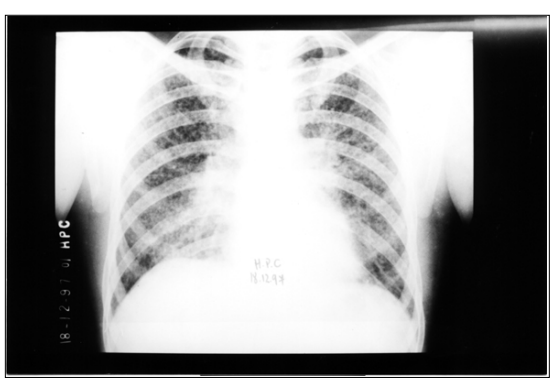

Figure 4 - Case 2 chest x-ray revealing diffuse and bilateral micronodular interstitial infiltrate.

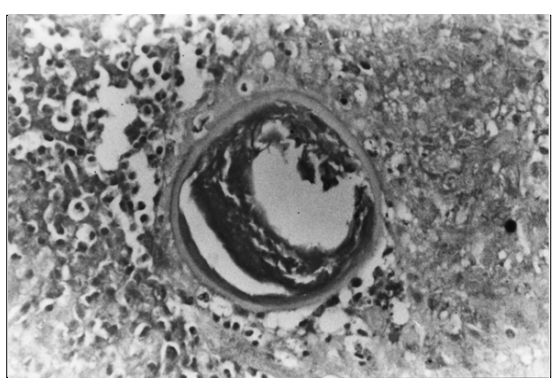

Figure 5 – Adiaconidium in granuloma center, with periodic acid Schiff positive trilaminar wall and containing eosinophilic granular material (PAS, 400X).

and the inner not stained by eosin, centrally empty and surrounded by a fibrogranulomatous response with Langhans' giant cells, aspect compatible with *Emmonsia parva* var *crescens*. No mycobacteria or fungi were cultured from the samples obtained from bronchoalveolar lavage aspirate and from pulmonary tissue.

Patient was followed up in the outpatient service and did not use the prescribed ketoconazole. On 08/27/98, he was in a good health, and spirometry showed a mild restrictive disturbance with FVC: 4,020ml (82.7%, predicted 4,860ml)[26]. The chest x-ray and CT films showed a clear improvement of the pulmonary lesions, and only a very discrete micro nodular infiltrate was observed (Figure 6).

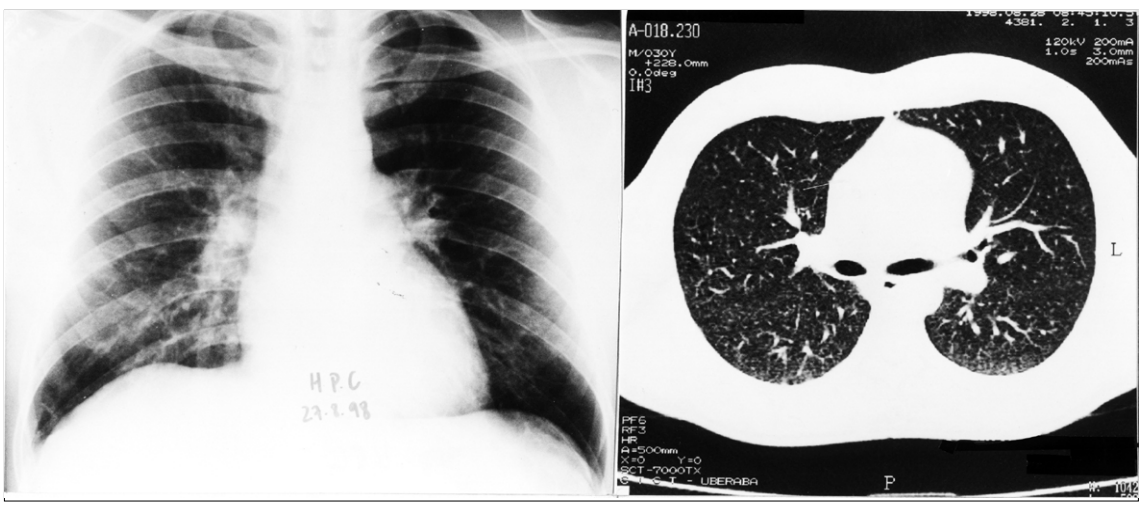

Figure 6 – Case 2 control chest x-ray and CT showing only a very discrete micronodular infiltrate.

DISCUSSION

As demonstrated in Table 1, which includes a case previously reported by the authors[24], all the patients were farm workers engaged in outdoor activities exposed to dust and, therefore, at risk of *Emmonsia* conidia inhaling. In our cases, clinical complaints started from August to December, which is a period characterized by warm dry climate and high winds[19]. Two of the patients were cigarette smokers. There was no evidence of associated diseases nor immunosuppression. All the patients referred *grippe-like* symptoms and, due to pulmonary lesions radiographic appearance, they had been treated for atypical pneumonia or miliary tuberculosis. Leukocytosis, neutrophilia and pulmonary reticular and micronodular infiltrate were observed in all the cases. Patients lung function was measured by spirometry, and revealed moderate to severe restrictive disturbances which, without apparent functional sequelae, returned to normality concomitant with the patients clinical cure, about a month later.

Table 1 - Comparative data from three cases of pulmonary adiaspiromycosis diagnosed in Uberaba, MG, from August 94 to December 97.

Patients	Date	Profession	Chest x-ray	ttc biopsy	tbr biopsy	Azole	Evolution
BGO, m, w, 26y	Aug, 94	farm worker	miliary	positive	negative	yes	cure
EB, m, w, 54y	Sept, 97	farm worker	miliary	positive	negative	yes	cure
HPC, m, w, 29y	Dec, 97	farm worker	miliary	positive	positive	no	cure

m: male; w: white; y: years; ttc: transthoracoscopic; tbr: transbronchial; azole: ketoconazole.

On the contrary to other reports[3,18], transbronchial biopsy was less useful than transthoracoscopic biopsy to render a specific diagnosis of pulmonary adiaspiromycosis in our patients. Both procedures were performed in all the cases, however, only in case 2 the lung tissue samples obtained via transbronchial revealed the presence of adiaconidia[4,6,12,15,24].

In the present cases, an azole compound was prescribed to patients with the pulmonary disseminated form of disease[20,21,24,27]. Although one of these did not use the drug prescribed, both cases similarly improved very well within a month, favoring the possibility of spontaneous regression of the pulmonary lesions, even in cases of symptomatic disseminated disease.

The etiologic agent of adiaspiromycosis belongs to class *Hyphomycetes*, genus *Emmonsia* or *Chrysosporium* related to *Ajellomyces*, family *Onygenaceae*, including *Blastomyces dermatitides* and *Histoplasma capsulatum*[5,7,16,25]. Fungi pertaining to the genus *Chrysosporium* have been described in samples from soil and lung tissue of burrowing mammals[23], especially rodents, in wild and urban-peripheric areas, with a world-wide-distribution[13,22].

It is well known that farm activities may expose humans to soil dust containing conidia fungus; however, case reports of symptomatic human adiaspiromycosis or incidental necropsy findings persist astonishingly rare, even in countries where unhealthy agricultural and rural activities still predominate. It is possible that this infection may be more frequent than reported, with a subclinical evolution, besides being misdiagnosed as *grippe*, pneumonia, miliary tuberculosis, another mycosis and conditions causing reticular and nodular lung infiltration.

Factors that may impede the diagnosis of human pulmonary adiaspiromycosis include very limited knowledge about this disease, asymptomatic infections or non specific clinical manifestations, chest x-ray appearance similar to other pulmonary diseases, lack of a specific serologic test, culture of the fungus not available, inadequate lung tissue samples, and the possibility of spontaneous cure in almost all cases.

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