Acute pulmonary adiaspiromycosis. Report of three cases and a review of 16 other cases collected from the literature

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Summary

We describe three cases of adiaspiromycosis with acute clinical menifestations and diffuse lung lesions. Sixteen previously reported similar cases are also reviewed. The best designation for this syndrome is acute pulmonary adiaspiromycosis.

Key words

Adiaspiromycosis, Acute pulmonary infection, *Emmonsia parva*

Adiaspiromicosis pulmonar aguda. Relato de tres casos y revisión de otros 16 casos obtenidos de la literatura

Resumen

Se describen tres casos de adiaspiromicosis con manifestaciones clínicas agudas y lesiones pulmonares difusas. Dieciséis casos similares relatados previamente son también revisados. La mejor designación para esta síndrome es adiaspiromicosis pulmonar aguda.

Palabras clave

Adiaspiromicosis, Infección pulmonar aguda, *Emmonsia parva*

Adiaspiromycosis is a world wide airborne infection due to *Emmonsia parva*. The disease afflicts man and small animals, specially rodents. In the pulmonary tissue of the host, an inhaled conidium enlarges, to become an adiaconidium. As adiaconidia do not duplicate, the lesions are usually limited to the lungs and the symptomatology and radiological findings are directly related to the number of inhaled conidia. A small inoculum produces no or mild clinical symptoms and scattered radiological pathology. But those individuals submitted to an heavy or repeated inoculum may present an acute, sometimes severe, pulmonary disease, with granulomatous lesions distributed randomly throughout both lungs.

In this report three cases of acute pulmonary adiaspiromycosis are described. Sixteen similar cases gathered from the literature will be summarized.

METHODS

The diagnostic criteria of acute pulmonary adiaspiromycosis include: 1) an acute onset of respiratory and systemic symptoms, 2) a radiological picture of diffuse micronodular lesions in both lungs, and, 3) histopathological demonstration of the adiaconidia in the granulomas.

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Aceptado para publicación el 6 de mayo de 1997

CASES REPORT

Case 1. A 52 year-old, caucasian man, from Itapetinga, Bahia, was admitted to the hospital with cough, mucoid expectoration, fever, and weight loss over the previous five months. He presented with a chest roentgenogram that showed diffuse micronodular infiltrates. He was treated for two months with antituberculous drugs, without improvement. In the immunodiffusion test with histoplasmin an M band was detected. A transbronchial biopsy was performed; in the H&E stained sections some structures like helminths were seen. Subsequently an open lung biopsy was performed. Sections were referred to a mycologist; special stains for fungi were done which revealed granulomas and characteristic adiaconidia (Figure 1). Serum of the patient was sent to the Center for Diseases Control and Prevention (Atlanta, USA) which confirmed the M band in immunodiffusion test and reported that the complement fixation test for histoplasmosis had a title of 1:8 (CDC 92-002417). The patient improved symptomatically without treatment.

Comment. The detection of an M precipitin band indicates a double infection or an old *Histoplasma capsulatum* infection (Leo Kaufman, personal comunication). Furthermore, earlier studies have shown that in skin test surveys there were individuals positive for both histoplasmin and haplosporangin [1].

Case 2. This patient was a 47 year-old, white man, from Irecê, Bahia. He was admitted with nonproductive cough, dyspnoea, fever, and weight loss. A chest roentgenogram revealed diffuse interstitial infiltrates in both lungs. Under suspicion of sarcoidosis, histoplasmosis or miliary tuberculosis, the patient was submitted to a trans-

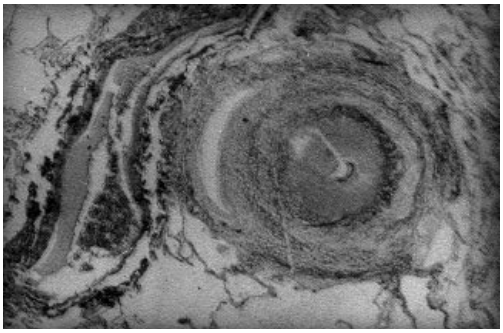

Figure 1. Case 1, a bronchiolocentric granuloma with an adiaconidium (PAS 20x).

bronchial biopsy. Two granulomas, one of which contained an adiaconidium were observed in H&E stained sections (Figure 2); sections stained by Gomori methenamine silver outlined the fungal structure measuring 100 µm, in diameter. The patient recovered without treatment.

Comment. In spite of the small tissue specimen, the presence of a single but characteristic adiaconidium may be diagnostic.

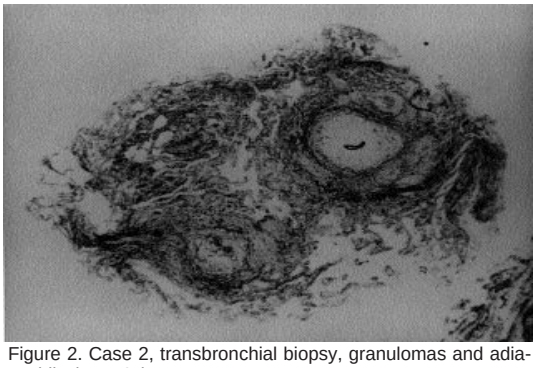

Figure 2. Case 2, transbronchial biopsy, granulomas and adiaconidia (H&E 8x).

Case 3. A 43 year-old white man, living in General Camara, Rio Grande do Sul, was admitted with a one-month history of fever (39.5°C), cough with scant expectoration, weight loss (3 Kg), dyspnoea and thoracic pain. A chest roentgenogram revealed bilateral micronodular infiltrates (Figure 3). Sputum examination for malignant cells, acid-fast bacilli, and fungi were negative. No precipitin band against histoplasmin was obtained in an immunodiffusion test. A bronchoalveolar lavage specimen did not reveal acid-fast bacilli or fungi. A tuberculin skin test (PPD) was also negative. Nevertheless, on the base of clinical and radiological features the patient was treated for tuberculosis. Because the patient did not improve a transbronchial biopsy was performed. Granulomas with characteristic adiaconidia were observed in H&E stained sections. An oriented epidemiological history disclosed that the patient had disrupted two mice nests, in a farm, fourteen days before becoming ill. He was treated with itraconazole 200 mg/day for a week without clinical improvemen. Prednisone (30 mg/day) was then added to the antifungal treatment; in a week the patient was asymptomatic.

Comment. The association of a steroid with the antifungal drug seems to be very important for clinical recovery. It disminishes the tissular inflammatory response, facilitating the action of the fungal drug. Ketoconazole alone led to cure in another patient [2], but further investigations are needed to establish an effective therapeutic protocol.

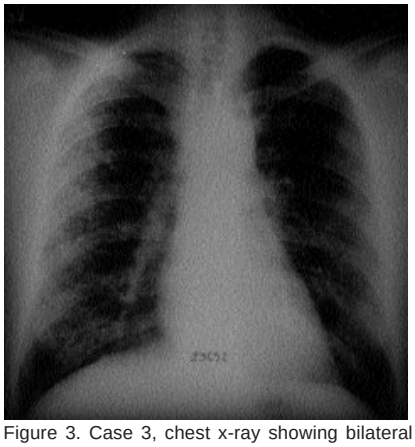

Figure 3. Case 3, chest x-ray showing bilateral micronodular infiltration.

DISCUSSION

Lesions of adiaspiromycosis are usually confined to the lungs. Exceptionally, extrapulmonary organs may be affected [3]. The first case of adiaspiromycosis was published in France in 1964. There was a solitary pulmonary nodule, detected incidentally in a patient's lung resected for bullae colonized by *Aspergillus* [4]. In the majority of reported cases, the mycosis was self-limited, discovered by chance in asymptomatic patients, as with the first Brazilian case [5].

In 1971, Kodousek [6] described the first case of a patient presenting symptoms of respiratory infection due to diffuse bilateral lung lesions. Since then overt adiaspiromycosis has been designated "primary progressive pulmonary" or "disseminated pulmonary adiaspiromycosis". We prefer to name similar conditions "acute pulmonary adiaspiromycosis", to distinguish from other clinical syndromes (histoplasmosis, coccidioidomycosis, Hodgkin's disease, sarcoidosis) with which it may be confused.

Twenty eight cases of acute pulmonary adiaspiromycosis have been collected from the available literature [2,6-17]. Nine of these cases [17], however, cannot be discussed, because individual case histories were not provided. Summarized data of the remaining nineteen cases are presented in the table. Sixteen of these cases occurred in Brazil [2,9-16, cases 1-3].

All human cases of adiaspiromycosis have been ascribed to *Emmonsia parva* var. *crescens.* This variety is also the most frequent agent of the mycosis in small animals, the reservoir host of the fungus. The inhalation of a great number of conidia causes the acute pulmonary form of the mycosis and has been related to cleaning [13,16, case 3] or playing [2,8] in long time closed environments inhabited only by bats and mice.

The diagnosis of pulmonary adiaspiromycosis is difficult. It cannot be made with the usual specimens collected for establishing the aetiology of respiratory infections. Adiaconidia are not seen or isolated in culture from sputum or bronchoalveolar fluid, because they do not multiply and remain trapped within lung granulomas. The diagnosis is usually achieved by chance, in specimens of biopsied lung tissue stained routinely by H&E.

Table 1. Clinical features of 19 patients with acute pulmonary adiaspiromycosis.

Author, year	Country	Age, sex	Symptoms and signs	Clinical hypothesis	Diagnostic approach			Therapy, outcome
					Material	Histologic	Culture	
KODOUSEK, 1971	Czechoslovakia	11, M	Fever,nonproductive cough, and dyspnea.	Tuberculosis, sarcoidosis	OLB	+	ND	Prednisone, improved
QUILICI, 1976	France	7, M	?	Tuberculosis, Hodgkin's disease	OLB	+	-	?
QUILICI, 1977	France	5, M	Astenia, headache, fever, and weight loss.	Tuberculosis, Hodgkin's disease	OLB	+ (*)	ND	Amp B, 5FC, improved
NUNES, 1986	Brazil	?, M	Nonproductive cough, dyspnea, cyanosis, and fever.	Virus pneumonia	Autopsy	+	ND	None, died
CAVALLARI,1986	Brazil	37, M	?	?	OLB	+	ND	None , Improved
SEVERO, 1989	Brazil	37, M	Fever, dyspnea, cough with scant expectoration, anorexia, weight loss, and prostration.	Histoplasmosis	OLB	+	-	Ketoconazole, improved
MORAES, 1989	Brazil	31, M	Fever, nonproductive cough, dyspnea, weight loss, muscular pain, chills, and malaise.	Malaria, tuberculosis	Autopsy	+	ND	None, died
MORAES, 1990	Brazil	42, M	Fever, dyspnea, nonproductive cough, chills, and weight loss.	Tuberculosis, paracoccidioidomycosis	OLB	+	-	Ketoconazole, improved
BARBAS, 1990	Brazil	42, M	Dyspnea, fatigue, fever, night sweats, and nonproductive cough.	Tuberculosis	OLB	+ (*)	ND	None, improved
		29, M	Dyspnea, coryza, myalgia, anorexia, fever, headache, and nonproductive cough.	?	TBB, OLB	+ (*)	ND	None, improved
TEIXEIRA, 1991	Brazil	62, M	Nonproductive cough and fever.	?	OLD	+	ND	Amp B, Improved
		30, M	Fever, cough with scant expectoration, chills, and thoracic pain.	Tuberculosis	OLB	+	ND	Amp B, predinisone, improved
		32, M	Fever, chills, thoracic pain, nonproductive cough and dyspnea.	?	OLB	+	ND	None, improved
		60, M	Fever, cough, purulent sputum, and weight loss.	Tuberculosis	OLB	+	ND	None, improved
LEME, 1992	Brazil	40, M	Fever, productive cough, anorexia, and weight loss.	Tuberculosis	OLB	+	ND	None, improved
PERES, 1992	Brazil	35, M	Weakness, myalgia, nonproductive cough, fever, shivering, weight loss, and dyspnea.	Tuberculosis, paracoccidioidomycosis	Autopsy	+	ND	None, died
This report, 1996	Brazil	52, M	Cough, mucoid sputum, fever, and weigh loss.	Tuberculosis	TBB, OLB	+ (*)	ND	None, improved
		47, M	Nonproductive cough, dyspnea, fever and weigh loss.	Sarcoidosis, histoplasmosis, tuberculosis	TBB	+	ND	None, improved
		43, M	Fever, cough, scant expectoration, weight loss,dyspnea, and thoracic pain.	Histoplasmosis, tuberculosis	TBB	+	ND	Itraconazole, prednisone, improved

(*) Initially interpreted as helminthic infestation; OLB: open lung biopsy; TBB: transbronchial biopsy; ND: not done.

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