

# Original Article

## Coexistence of intracavitary fungal colonization (fungus ball) and active tuberculosis\*

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**Background:** Although pulmonary tuberculosis is the principal predisposing factor for intracavitary fungal colonization, the coexistence of the two diseases is rare. Simultaneity of fungal colonization and active mycobacteriosis in the same cavity (acid-fast bacilli found among hyphal masses) is highly unusual.

**Objective:** To describe clinical findings, diagnostic procedures, radiographic aspects, accompanying conditions and evolution in patients with tuberculosis and fungus ball.

**Method:** We reviewed, retrospectively, the records of 625 patients diagnosed with fungus ball between 1974 and 2002. All of the patients had been diagnosed through immunodiffusion or mycological study, or both. The inclusion criterion was positivity for acid-fast bacilli in sputum smear microscopy or histopathology.

**Results:** The charts of 14 patients were selected. All had presented hemoptysis, followed by productive cough, dyspnea, weight loss, fever, asthenia and chest pain. In one patient colonized by *Aspergillus niger* and in another colonized by *Scedosporium apiospermum* (Teleomorph, *Pseudallescheria boydii*), active tuberculosis was seen concomitant to the fungus ball. In the remaining cases, the mycobacteria were found in the adjacent parenchyma or in the contralateral lung.

**Conclusion:** This study corroborates the assertion that antagonism exists between *Mycobacterium tuberculosis* and *Aspergillus fumigatus*. The potential for fungal colonization and mycobacteriosis to occur concomitantly is demonstrated in other fungal agents, *S. apiospermum* (*P. boydii*) and *A. niger* in particular.

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**Key words:** Aspergillosis. *Aspergillus fumigatus*. *Aspergillus niger*. *Pseudallescheria*. *Mycobacterium tuberculosis*. *Scedosporium apiospermum*.

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## INTRODUCTION

The predominant etiologic agent of pulmonary intracavitary fungal colonization (fungus ball) is *Aspergillus fumigatus*, and a healed tuberculous cavity is the principal predisposing factor. In the latter, pericavitary fibrosis and endocavitary epithelization, which derives from the bronchial connections, hinder phagocytosis of the fungal propagules, thereby making colonization possible. The mucus present on the bronchial epithelium provides the culture<sup>(1,2)</sup>.

The rarity of fungal colonization concomitant with active tuberculosis<sup>(3)</sup> justifies the present study.

## METHODS

We reviewed the records of 625 patients diagnosed with fungus ball in the city of Porto Alegre (RS) between 1974 and 2002. The inclusion criteria were positive microscopy for bacilli and radiographic images suggestive of fungus ball. Etiologic evidence of fungal colonization was obtained through mycological blood culture (double radial immunodiffusion) using specific antigens or through standard mycological diagnosis (microscopy and culture), or both. The cases were characterized in terms of clinical data (gender, age, principal symptoms, comorbidities, radiographic aspects, treatment and evolution), diagnostic procedures, therapeutic aspects and evolution.

## RESULTS

A total of 14 patients (2%) fulfilled the inclusion criteria. All were male and between 29 and 66 years of age. In addition to tuberculosis, the majority presented other comorbidities: 6 (42%) were alcoholics, 2 (14%) were smokers, 2 (14%) presented chronic obstructive pulmonary disease, 2 (14%) were diabetics, 1 (7%) had hepatitis and 1 (7%) suffered from oligophrenia.

All patients presented hemoptysis. Other manifestations included the following: cough (86%), purulent expectoration (79%), dyspnea (43%), weight loss (43%), fever (29%), asthenia (21%) and chest pain (14%) (Table 1).

The most common radiographic finding was intracavitary content, mostly in the upper lobes, suggestive of fungus ball. This was found in 86% of the cases. All patients presented complex fungus ball. In patients colonized by *A. fumigatus*, there were contralateral lesions suggestive of active tuberculosis. In patients colonized by *A. niger*, the lesions were ipsilateral, and only in one case (Case 1) were lesions seen concomitant to the fungus ball. One patient (Case 14) was colonized by *Scedosporium apiospermum* (Teleomorph, *Pseudallescheria boydii*) and also presented concomitant tuberculous and fungal lesions (Table 2).

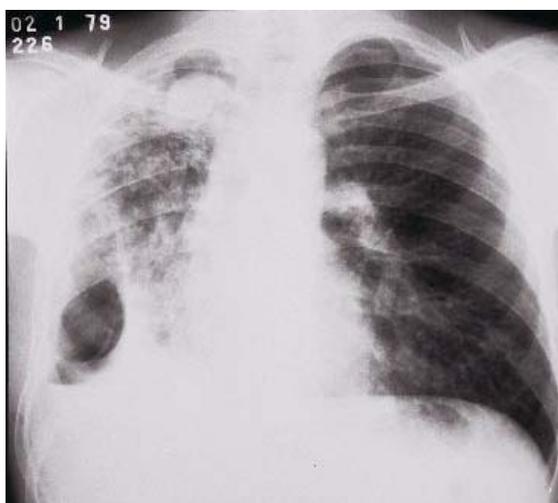
TABLE 1

Clinical characteristics of patients with fungus ball and tuberculosis

Case	Age	Clinical manifestations		Comorbidities*
		H/C/E	Other symptoms	
1	49	+ /+ /+	Weight loss, asthenia	Alcoholism, DM, oxalosis
2	38	+ /+ /+	Dyspnea, chest pain	Alcoholism, COPD
3	34	+ /+ /+	Fever	Oligophrenia
4	49	+ /+ /+	Dyspnea, cyanosis, anorexia	COPD
5	55	+ /+ /+	Weight loss, chest pain, dyspnea	NWN
6	59	+ /- /-	No other complaints	Alcoholism, smoking, DM
7	40	+ /- /-	Dyspnea	Smoking
8	31	+ /+ /+	No other complaints	Alcoholism, hepatitis
9	46	+ /+ /+	Weight loss	NWN
10	29	+ /+ /+	Fever, weight loss, asthenia	NWN
11	56	+ /+ /BF	Chest pain, dyspnea	NWN
12	58	+ /+ /+	Weight loss	Alcoholism
13	44	+ /+ /+	No other complaints	Alcoholism
14	66	+ /+ /+	Dyspnea, fever, asthenia, weight loss	NWN

\*other than tuberculosis

H: hemoptysis; C: cough; E: expectoration; BF: expectoration with fragments of fungus ball; DM: diabetes mellitus; COPD: chronic obstructive pulmonary disease; NWN: nothing worthy of note; AFB: acid-fast bacilli



**Figure 1.** Chest X-ray (Case 10) showing a thick-walled cavity (4.5 x 3.5 x 2.5 cm) containing pathological material with dense soft parts (fungus ball) in the apical segment of the upper lobe of the right lung. In the lateral-inferior portion of the hemithorax, a secretion-filled septal cavity, resulting from a pyopneumothorax pustule with bronchial fistula, can be seen. Smear microscopy of the pus was positive, and the agent was identified as *M. tuberculosis*.

Etiologic evidence of fungal colonization was obtained through mycological blood culture in 11 patients (79%) who were unfit for surgery, surgical sample in 2 patients (Cases 9 and 10), biopsy material obtained by fiberoptic bronchoscopy in 1 patient (Case 1) and autopsy in 1 patient (Case 14). Microscopy (for acid-fast bacilli) was used to confirm the diagnosis of mycobacteriosis in 12 patients. Positive culture for *Mycobacterium tuberculosis* was obtained in only 2 patients (Cases 1 and 14).

The most prevalent fungus was *A. fumigatus* (57%; Cases 6 to 13), followed by *A. niger* (29%; Cases 1 to 4), *A. flavus* (7%; Case 5) and *S. apiospermum* (7%; Case 14). A total of 12 patients (Cases 2 to 13) presented fungus ball in healed cavities, and 3 patients undergoing surgery (Cases 9, 10 and 13) presented positivity for acid-fast bacilli in microscopy of adjacent parenchyma. In Case 1 (*A. niger*) and Case 14 (*S. apiospermum*), fungal colonization occurred in an active cavity (positivity for *M. tuberculosis* in microscopy and culture) (Table 3).

TABLE 2

Fungus ball and tuberculosis: radiographic aspects

Case	Lesion location	Radiographic findings
1	Both lungs	Excavated consolidation in the URL, with contralateral bronchial dissemination. FB in the LRL
2	Right lung	Destroyed right lung, cavities with FBs
3	Upper lobes	Wide bilateral cavities: one with FB on the left and one with AFL on the right
4	Left lung	Destroyed left portion of the lung, cavities with FBs
5	Upper right lobe	Cavity with FB
6	Upper right lobe	Cavity with FB
7	Left lung	Destroyed left lung with FB
8	Upper lobes	Cavities with FB in the URL; lesions on the left suggestive of active tuberculosis in the ULL
9	Upper lobes	Bilateral fibroatelectasis retractions, cavity with FB in the URL
10	Upper lobes	Cavity with FB in the URL, ipsilateral empyema
11	Upper lobes	Bilateral pleural thickening, cavities in bilateral apices, with FBs
12	Left lung and upper right lobe	Destroyed left lung with FB in the LLL; cavity with FB in the URL
13	Left lung	Destroyed left lung, with FB in the ULL. Exudative lesions in URL and sites of bronchogenic dissemination in ML and LRL
14	Both lungs	Lesions in both lungs with areas of consolidation and emphysema, cavity with AFL in URL

URL: upper right lobe; FB: fungus ball; LRL: lower right lobe; AFL: air-fluid level; ULL: upper left lobe; LLL: lower left lobe; ML: middle lobe.

TABLE 3

Etiologic documentation of fungal colonization and mycobacteriosis

Agent	Case	Mycosis		Mycobacteriosis	
		DI	Culture	AFB	Culture
Aspergillus fumigatus	6	+	NP	sputum	NP
	7	+	NP	sputum	NP
	8	+	NP	sputum	NP
	9	+	-	surgical sample	NP
	10	+	NP	pleural empyema	M. tuberculosis
	11	+	NP	sputum	NP
	12	+	NP	sputum	NP
	13	+	NP	sputum	NP
Aspergillus niger	1	+	+	byopsy	M. Tuberculosis
	2	+	NP	sputum	NP
	3	+	NP	sputum	NP
	4	+	NP	sputum	NP
Aspergillus flavus	5	+	NP	sputum	NP
Scedosporium apiospermum *	14	+	+	autopsy	

\*Teleomorph, *Pseudallescheria boydii*

DI: immunodiffusion; AFB: acid-fast bacilli; NP: not performed

Only 3 patients received surgical treatment, undergoing lobectomy (Case 9) or pneumonectomy (Cases 10 and 13). One patient (Case 2) was submitted to radiotherapy due to hemoptysis severity. Ten patients received tuberculostatic treatment.

Clinical follow-up examinations were performed in 12 cases. Among these patients, 6 died: 3 of hemoptysis, 1 of acute oxalosis and 2 of undetermined causes.

## DISCUSSION

Since the first studies on pulmonary intracavitary fungal colonization were carried out, *A. fumigatus* has been documented as the fungus that is most frequently involved, appearing in healed cavities<sup>(2)</sup>. The antagonism between this agent and *M. tuberculosis* is demonstrated by the production of metabolites, such as fumagillin, fumitoxin and gliotoxin, that inhibit mycobacterial growth<sup>(4)</sup>. The present study clinically corroborates this antagonism, demonstrating that, in cases in which the two diseases occurred concomitantly, there was no spatial coincidence. Although Adeyemo et al.<sup>(5)</sup> drew attention to the simultaneity of fungus ball and active tuberculosis, they found

no evidence of lesion simultaneity or of fungal etiology of the colonization. Other studies describing concomitance between fungus ball and tuberculosis were also unclear regarding the simultaneity of both agents in the same lesion<sup>(1)</sup>.

Excluding *A. fumigatus*, the potential for fungal colonization and mycobacteriosis to coexist is questioned<sup>(6-10)</sup>. Cases 1 and 14, published separately<sup>(11, 12)</sup>, presented lesions concomitant with pathological anatomy, with fungal and mycobacterial viability, demonstrating this potential in fungal agents other than *A. fumigatus*.

Surgery is the treatment of choice for fungus ball. In the present study, surgical treatment was possible in only 3 cases. In patients who present concomitant active tuberculosis, a negative sputum smear is considered a prerequisite to surgery, except in emergency cases<sup>(13)</sup>. Another factor that limited the number of surgical procedures was the fact that all cases in the present study presented complex fungus balls<sup>(14)</sup>.

In conclusion, we have demonstrated that it is possible for fungus ball and active tuberculosis to occur concomitantly at the same site since the colonizing fungal agents do not produce metabolites that can inactivate the mycobacterium.

## REFERENCES

1. Severo LC. Colonização intracavitária pulmonar por *Aspergillus niger*. Análise de suas peculiaridades. [Tese de doutorado]. Porto Alegre: Universidade Federal do Rio Grande do Sul - UFRGS, 1987.
2. Severo LC, Geyer GR, Porto NS. Pulmonary aspergillus intracavitary colonization (PAIC). *Mycopathologia* 1990; 112: 93-104.
3. Rippon JW. Aspergillosis. In: Wonsiewicz M, editor. *Medical mycology. The pathogenic fungi and pathogenic actinomycetes*. 3<sup>rd</sup> ed. Philadelphia: W.B. Saunders Company, 1988; 616-50.
4. Eichner RD, Mullbacher A. Hypothesis: fungal toxins are involved in aspergillosis and AIDS. *Aust J Exp Biol Med Sci* 1984; 62:479-84.
5. Adeyemo AO, Odelowo EO, Makanjuola DI. Management of pulmonary aspergilloma in the presence of active tuberculosis. *Thorax* 1984; 39: 862-7.
6. Lamy P, Anthoine D, Vaillant G, Monneau JP, Froment J, Neimann JL. Les aspergilloses bronchopulmonaires. *Ann Med Nancy* 1971; 10: 1369-80.
7. Retamal C, Díaz C, Salamarca L, Ferrada L, Oro RA. Aspergillosis pulmonar en Chile enfoque inmunológico. *Bol Micol* 1984; 2:11-6.
8. Renouf JP. L'aspergillome pulmonaire secondaire. A propos d'une observation. [These Doctorat]. Faculte de Medicine Paris Ouest, 1974.
9. Villar TG, Pimentel JC. Personal experience with pulmonary aspergillomas. *Bull Int Union Tuberc* 1970; 43:117-8.
10. Voisin C, Biguet J. L'aspergillose dans les lesions pulmonaires residuelles: problemes, diagnostiques, pronostiques et therapeutiques. *Bull Int Union Tuberc* 1970; 43: 119-20.
11. Severo LC, Londero AT, Picon PD, Rizzon CFC, Tarasconi, JC. *Petriellidium boydii* fungus ball in a patient with active tuberculosis. *Mycopathologia* 1982; 77: 13-7.
12. Severo LC, Geyer GR, Porto NS, Wagner MB, Londero AT. Pulmonary *Aspergillus niger* intracavitary colonization. Report of 23 cases and a review of the literature. *Rev Iberoam Micol* 1997; 14: 104-10.
13. Freixinet J, Rivas JJ, Castro FR, Caminero JA, Rodriguez P, Serra M, La Torre M, Santana N, Canalis E. Role of surgery in pulmonary tuberculosis. *Med Sci Monit* 2002; 8: 782-6.
14. Denning DW, Riniotis K, Dobrashian R, Sambatakou H. Chronic cavitary and fibrosing pulmonary and pleural aspergillosis: case series, proposed nomenclature change, and review. *Clin Infect Dis* 2003; 37:S265-80.