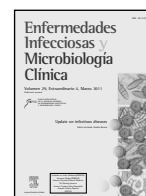




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Update on invasive mycoses by filamentous fungi in critically ill patients

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ABSTRACT

Keywords:

Invasive fungal infection
ICU
Moulds
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COPD

The present article is an update of the literature on invasive fungal infections caused by filamentous fungi in critically ill patients. A multidisciplinary group of Spanish physicians with an interest in these infections organized a joint session and selected the most important papers produced lately in the field. Each article was analyzed and discussed by one of the members of the panel. Studies from the fields of causative microorganisms, epidemiology, and diagnosis are discussed; including the assessment of different strategies for the early identification and treatment of patients at risk of fungal infections by filamentous fungi in the intensive care unit setting.

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Actualización en infección fúngica invasiva por hongos filamentosos en el paciente crítico

RESUMEN

Palabras clave:

Infección fúngica invasora
UCI
Mohos
Aspergillus
EPOC

El presente trabajo es una revisión de la bibliografía más relevante publicada recientemente acerca de la infección fúngica invasiva por hongos filamentosos en el paciente crítico. Un grupo multidisciplinar compuesto por diferentes especialistas españoles con interés en este campo ha seleccionado los artículos. Cada autor ha analizado y comentado una publicación, referente a la etiología, epidemiología y diagnóstico de las micosis profundas por hongos filamentosos. Además, se valoran las estrategias de diagnóstico y tratamiento precoz de estas graves infecciones en las unidades de cuidados intensivos.

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State of the art

Critical care medicine has improved greatly in the past few decades. Patients with complex medical and surgical disorders are surviving longer due to equally complex medical and surgical interventions. These often involve the “collateral damage” of circumventing the body’s normal defence mechanisms.

Approximately 10.4% of infections in an intensive care unit (ICU) are related to *Candida* spp., with the majority being nosocomial¹. However, this rate could be underestimated due to the fact that, at least in 4% of critically ill patients who die in an ICU, an unexpected fungal infection is found during postmortem examination². Although less frequent, aspergillosis (particularly in patients with chronic obstructive pulmonary disease)³⁻⁵ and other emergent molds and

yeasts, such as *Trichosporon asahii*, *Saccharomyces cerevisiae*, *Hansenula anomala*, *Dipodascus capitatus*, and *Rhizopus microsporus*, have been described in ICU patients during the last few years, and are associated with an increasing incidence of these infections in this subset of patients and a major impact on outcomes: a high morbidity and mortality and higher healthcare costs^{6,7}. Even dermatophyte infections have been described in ICU patients, mainly neonatal^{8,9}.

More recent analyses suggest that the epidemiology of invasive pulmonary aspergillosis (IPA) in the ICU may be shifting away from those traditionally considered at risk. Several recent case series have described IPA in nonimmunocompromised critically ill subjects, i.e. patients with chronic obstructive pulmonary disease (COPD)¹⁰. Poor outcomes are, in part, related with difficulties in establishing the microbiologic diagnosis at an early stage of infection. Blood culture results are positive in only 50% of invasive *Candida* spp. and *Fusarium* spp. infections, and are positive very rarely in cases of invasive aspergillosis (IA)¹¹. Cultures of bronchoalveolar lavage (BAL) fluid or brushing specimens are positive in <50% of subjects with IPA. Finally,

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positive cultures of specimens from nonsterile body sites may be related to either colonization or infection, and distinguishing between these two can be complex. However, nonculture-based diagnostic tests may provide a useful addition to these more traditional approaches. Of these, detection of galactomannan has appeared promising and could be useful to guide pre-emptive therapy¹². The present article is an update on the literature on invasive fungal infections caused by filamentous fungi in critically ill patients. Studies from the fields of causative microorganisms, epidemiology, and diagnosis are discussed; including the assessment of different strategies for the early identification and treatment of patients at risk of fungal infections by filamentous fungi in the ICU setting.

Update of the literature

Cornillet A, Camus C, Nimubona S, Gandemer V, Tattevin P, Belleguic C, et al. Comparison of epidemiological, clinical, and biological features of invasive aspergillosis in neutropenic and nonneutropenic patients: a 6-year survey. *Clin Infect Dis.* 2006; 43:577-84.¹³

IA is an opportunistic infection that occurs mainly among patients with prolonged neutropenia. The mortality rate exceeds 50% and can reach 90% in allogeneic hematopoietic stem cell transplant (HSCT) recipients. During the last decade, the management of IA in neutropenic patients has improved with the advent of new diagnostic tools and new antifungal drugs.

Few data are available on IA in allogeneic hematopoietic stem cell transplant recipients after recovery from neutropenia or in patients who are free of hematological disorders and malignancies. However, IA can also occur after solid-organ transplantation or during long-term corticosteroid therapy and is an emerging opportunistic infection in patients with chronic respiratory disease.

At present there are no studies comparing neutropenic patients and nonneutropenic patients with IA. For this reason the Aspergillosis Study Group of Rennes Teaching Hospital (France) has recently published this study performed over a 6-year period (from January 1998 to December 2003) to characterize all patients diagnosed of IA in their institution. The study was retrospective for the period from January 1st 1998 through December 31st 1999 and prospective for the period from January 1st 2000 through December 31st 2003. Furthermore, the large proportion of nonneutropenic patients with IA gave the authors the opportunity to compare the diagnosis and therapeutic management of these patients with those of neutropenic patients. Cases of IA were classified as possible, probable, or proven on the basis of the classification system of the European Organization for Research and Treatment of Cancer/Mycosis Study Group (EORTC/MSG). Eighty-eight patients were enrolled during the study period. Twelve cases (14%) of IA were histologically proven, 52 (59%) were probable, and 24 (27%) were possible. Cases of IA were diagnosed mainly in the intensive care unit (47%) and the hematology unit (40%). Neutropenia was a risk factor for 52 patients (59%), most of whom had hematological or solid malignancies. Among the 36 (41%) nonneutropenic patients, the main underlying conditions were steroid-treated COPD, asthma, rheumatoid arthritis, giant-cell arteritis, and microvascular disorders; 10 patients were recipients of solid-organ transplants, and 1 patient was HIV positive. The distribution of proven and probable IA was similar for neutropenic and nonneutropenic patients. The overall mortality rate was 71.5% and was significantly higher among nonneutropenic patients than in neutropenic patients (89% vs. 60%; $P < .05$). Nonneutropenic patients were significantly less likely to have symptoms of IA and more likely to have frequent intercurrent pneumonia due to other microorganisms. The sensitivity of the mycological examination of BAL fluid specimens was higher for nonneutropenic patients than for neutropenic patients (85% vs. 58%) whereas the sensitivity of *Aspergillus* galactomannan antigenemia was comparable for both

populations. Findings on thoracic computed tomography were similar, except that segmental areas of consolidation occurred more frequently among neutropenic patients. Only 31% of the patients were treated with voriconazole.

Comments. This study demonstrates that the overall mortality rate due to IA was significantly higher in nonneutropenic patients than in neutropenic patients. Therefore, an important question arises after reading this paper: It is necessary to apply a score to identify and treat IA patients early on, especially those who are nonneutropenic. Moreover, some limitations must be taken into consideration. Data were collected more than five years ago, and at present the management of these patients has changed and possibly the results may not reflect the actual situation due to the fact that only 31% of the patients were treated with voriconazole, the actual first-line option to treat IA.

Bulpa P, Dive A, Sibille Y. Invasive pulmonary aspergillosis in patients with chronic obstructive pulmonary disease. *Eur Respir J.* 2007;30:782-800.¹⁴

Invasive pulmonary aspergillosis (IPA) is known to account for a large number of deaths in haematological and solid-organ transplant patients. According to recent autopsy series, its incidence has grown over the last decades, probably related to the increasing use of immunosuppressive and corticosteroid therapies in this patient population. *Aspergillus* spp. isolated in samples from the airway of patients with COPD is usually considered as a contaminant. However, growing evidence suggests that severe COPD patients are at higher risk of developing IPA, although IPA incidence in this population is poorly documented. The present review addresses the epidemiology and pathophysiology of IPA in 56 COPD patients reported in the literature¹⁴. It further discusses the early clinical signs observed in these patients, as well as the available diagnostic procedures, in order to facilitate rapid recognition and appropriate treatment.

Definitive diagnosis of IPA in COPD patients is often difficult as tissue samples are rarely obtained premortem. Diagnosis is usually based on a combination of clinical features, radiological findings (mostly thoracic CT scans), microbiological results and, sometimes, serological information. Most patients (77%) of this study were receiving corticosteroids on admission to hospital. Breathlessness was always a feature of the clinical presentation and excess wheezing was found in 79% of patients. In contrast to hematological patients, fever, chest pain and haemoptysis were uncommon. In 75% of patients, an elevated white blood cell count ($>12,000$ cells/mL) was identified. Tracheobronchitis was observed in 18% of patients and the median delay between symptoms and diagnosis was 8.5 days. Chest radiographs showed nonspecific consolidation images in 75% of cases, while specific images of IPA were observed only in 21% of patients. Thoracic CT scan was performed in 16 patients and in 11 of them contributed to IPA diagnosis. In addition, global mortality rate was very high (95%) despite invasive ventilation and antifungal treatment.

Comments. Although COPD patients may be colonised with *Aspergillus* spp., its presence in the sputum must not be minimized, especially in cases of antibiotic-resistant pneumonia. COPD is the underlying disease in 1% of patients with IPA and in COPD patients this mycoses currently carries a very poor prognosis. More studies need to be carried out in order to better identify *Aspergillus* infection in COPD patients. The role of steroids in predisposing to IPA, the existence of specific risk factors related to COPD patients, the performance of non-invasive diagnostic tests (antigenemia, antibody detection or molecular diagnosis), and the validation of voriconazole as first-line therapy are some of the important issues that require further clarification to improve the prognosis of this devastating disease.

Castón JJ, Linares MJ, Gallego C, Rivero A, Font P, Solís F, et al. Risk factors for pulmonary *Aspergillus terreus* infection in patients with positive culture for filamentous fungi. *Chest* 2007; 131:230-6.¹⁵

Among patients with IA, *Aspergillus terreus* infections have become a growing concern in the past few years because they are often refractory to treatment with amphotericin B and the available data indicate that this fungus may have differential epidemiologic features, a more aggressive clinical behavior, and a higher mortality rate than other *Aspergillus* spp. The objective of this study was to identify the clinical risk factors for both the isolation and the infection by invasive *A. terreus* in patients with positive culture findings for filamentous fungi from respiratory samples¹⁵. The authors present a retrospective cohort study in a single hospital, which included 505 isolates of filamentous fungi from significant respiratory samples of 332 patients over a period of 10 years (1994-2004). Patients were classified into 2 groups: colonized and infected (MSG and EORTC criteria) and 3 categories of risk factors related to isolation of and infection by this pathogen were studied: a) host factors; b) factors related to immunosuppression; and c) factors related to hospitalization.

The incidence of isolation of filamentous fungi was 1.73/10,000 patients per year, and patients most commonly affected were solid organ transplant or HSCT recipients (31%). *A. terreus* (9.1%) was the second most frequently isolated mold after *A. fumigatus* (59%). Prophylaxis with amphotericin B aerosols and mechanical ventilation behaved as risk factors for *A. terreus* isolation. Invasive infection occurred in 42% and 59% of patients with isolation of *A. fumigatus* and *A. terreus*, respectively. Transplantation was associated with a lower risk of *A. terreus* colonization and infection.

Comments. This study reflects a higher incidence of *A. terreus* than previously published, associated to prophylactic use of amphotericin B aerosols and mechanical ventilation. It would be desirable to specify if this high rate was related to outbreaks or it is a regular incidence rate. Additionally, these results should be confirmed by prospective studies to determine whether there is a causal relationship between the administration of amphotericin B aerosols and the increased frequency of *A. terreus* colonization and infection. In most cases, *A. terreus* must be considered as pathogen since it carries a high rate of infection and amphotericin B resistance compared to other *Aspergillus* species. Thus, when a filamentous fungus is isolated in patients who have previously received amphotericin B aerosols or who present with an acute respiratory failure requiring mechanical ventilation, especially if there are construction works within the hospital or nearby, early and aggressive antifungal therapy that does not include amphotericin B must be administered.

Guinea J, Torres-Narbona M, Gijón P, Muñoz P, Pozo F, Peláez T, et al. Pulmonary aspergillosis in patients with chronic obstructive pulmonary disease: incidence, risk factors, and outcome. *Clin Microbiol Infect.* 2010;16:870-77.¹⁶

The authors describe a large series of patients with chronic obstructive pulmonary disease (COPD) and probable IPA, and the risk factors and incidence of the disease in patients with isolation of *Aspergillus* from lower respiratory tract (LRT) samples. From 2000 to 2007, all patients admitted with COPD and isolation of *Aspergillus* at their institution, Hospital General Universitario "Gregorio Marañón", Madrid, Spain (n=239; 16.3/1,000 admissions), were retrospectively studied. Multivariate logistic regression and survival curves were used. Fifty-three patients had probable IPA (3.6 cases of IPA per 1000 COPD admissions). IPA affected at least 22.1% of patients with COPD and isolation of *Aspergillus* in culture. In 33 of the 53 patients with probable IPA, serum GM was determined; in 14 (42.4%) of these, the result was positive. Five variables were independent predictors of

IPA with statistical significance: admission to the ICU, chronic heart failure, antibiotic treatment received in the 3 months prior to admission, the accumulated dosage of corticosteroids equivalent to >700 mg prednisone received in the 3 months prior to admission, and the similar accumulated dosage of corticosteroids received from admission to the first clinical isolation of *Aspergillus*. Multivariate analysis gave an area under the curve of 0.925 (95%CI, 0.888-0.962; $P < .001$). The overall mean survival of the cohort was 64.1% (28.3% for IPA patients and 75.2% for non-IPA patients). The median number of days of survival was 48 (95%CI, 33.07-62.92). However, the authors found statistically significant differences between patients with IPA (29 days; 95%CI, 20.59-37.40) and patients without IPA (86 days; 95%CI, 61.13-110.86) (log rank, $P < .001$).

Comments. In order to minimize the limitations of diagnostic procedures and the overestimation of isolation of *Aspergillus* in patients with COPD, the authors studied the predictive variables for IPA in patients with COPD and isolation of *Aspergillus* in LRT samples. The analysis showed that, in patients with COPD and in poor clinical condition (ICU admission and chronic heart failure) who have received antibiotics and high accumulated dose of corticosteroids, the isolation of *Aspergillus* in LRT samples should suggest to physicians the performance of a CT scan and the initiation of anti-*Aspergillus* therapy. Further prospective studies evaluating the outcome of COPD patients with *Aspergillus* isolated from the LRT are required. The impact of early and adequate antifungal therapy in this population has to be assessed, and high-risk patients should be selected for preventive or early therapy.

Jensen J, Guinea J, Torres-Narbona M, Muñoz P, Peláez T, Bouza E. Post-surgical invasive aspergillosis: an uncommon and underappreciated entity. *J Infect.* 2010;60:162-7.¹⁷

Post-surgical invasive aspergillosis (PSIA) is an unusual and underestimated complication of surgery. It may occur after colonization of surgical sites by airborne *Aspergillus* conidia during surgery, or in the immediate postoperative period. In this study, the authors reviewed 7 cases of PSIA (1997-2006) in their institution and checked the air levels of *Aspergillus* conidia in the operating rooms and/or areas surrounding patients. PSIA accounted for 8.4% (n=83) of all cases of invasive aspergillosis. Patients had no classic predisposing conditions (wound infection n=4, mediastinitis n=2, and endotipsitis with endocarditis n=1). PSIA occurred sporadically after heart, thoracic, and vascular prosthetic surgery. *Aspergillus fumigatus* was involved in all cases. Median time from surgery to diagnosis was 25 days. GM was only positive (≥ 1 ng/mL) in 2 patients (endotipsitis with endocarditis and mediastinitis). Mortality was 100% in cases of organ/space post-surgical infections. Although the air of operating theatres taken before surgery was free of *Aspergillus*, airborne *Aspergillus* conidia levels were high (>95 CFU/m³) in the rooms of 2 patients.

Comments. PSIA represented almost 10% of all cases of invasive aspergillosis. Cases were not linked to high levels of *Aspergillus* conidia in the operating theatre but to postoperative contamination by environmental isolates present in high counts.

The duration of antifungal treatment and the agent of choice for patients with PSIA remain unresolved. After reviewing several case reports, Pasqualotto and Denning recommended that, once as much infected tissue as possible has been debrided, antifungal treatment should be administered for no less than 3 months beyond the last evidence of active disease¹⁸. Although no prospective studies show the superiority of voriconazole in patients with PSIA, new IDSA guidelines recommend its use¹⁹. Patients in this study received a mean of 6 weeks of antifungal treatment, mainly with itraconazole, after debridement. Outcome was favorable after 1 year of follow-up.

Meersseman W, Lagrou K, Maertens J, Wilmer A, Hermans G, Vanderschueren S, et al. Galactomannan in broncho-alveolar lavage fluid: a tool for diagnosing aspergillosis in ICU patients. *Am J Respir Crit Care Med.* 2008;177:27-34.²⁰

IA may be an underestimated opportunistic fungal infection in critically ill patients, even in the absence of haematological malignancy. Patients with chronic obstructive pulmonary disease, liver cirrhosis, patients on steroids, and solid transplant recipients, are especially at risk and were not included in the original criteria for definition of proven and probable IA according to the widely accepted EORTC-IFIG/MSG guidelines.

Galactomannan antigen (GM) is released by *Aspergillus* during fungal growth, and its detection by sandwich-enzyme immunoassay (EIA) has been approved for use in HSCT recipients, but there are few data in different subsets of patients. The authors conducted this prospective trial in critically ill patients at risk for IA and compared the diagnostic performances of GM detection in BAL, radiological signs, culture results, and serum GM detection²⁰.

A total of 110 patients were enrolled during the study period. Following post-mortem examination, study patients were classified as proven IA (24%), probable IA (7%), possible IA (24%), proven non-*Aspergillus* mould infection (3%), colonization (3%) and no IA (39%). Only 4 out of the 26 proven cases were diagnosed as proven IA pre-mortem. Using a cut-off index of 0.5, the sensitivity and specificity of GM detection in BAL fluid was 88% and 87%, respectively. The sensitivity of serum GM was only 42%. In 11 of 26 proven cases BAL culture and serum GM remained negative while GM in BAL was positive.

The good results obtained in BAL samples in these patients (88% nonneutropenic) with a cut-off index of 0.5 differ from those of previous studies in solid organ (SOT) and lung transplant (LT) recipients, which recommend a higher cut-off index for BAL. A recent study about the role of GM antigen in BAL in the early diagnosis of IA in LT recipients found that a cut-off index value of ≥ 0.5 showed a sensitivity of 60% and a specificity of 95%. Increasing the index cut-off value to ≥ 1.0 yielded the same sensitivity and a specificity of 98%²¹. Therefore, a cut-off index of ≥ 1.0 in BAL fluid in LT recipients with a compatible clinical illness may be used for the diagnosis of IA.

In another study performed in SOT patients, GM test in BAL had an excellent specificity (90.8% with a cut-off index of ≥ 1.0). The sensitivity of BAL GM testing was 100%, compared to 50%, 40%, and 25% for cytology, culture, and transbronchial biopsy results, respectively, and 25% for serum GM levels of ≥ 0.5 ²². LT recipients accounted for almost half of all false-positive test results (41.7% with a cut-off index of ≥ 0.5 and 42.9% with a cut-off index of ≥ 1.0). The high rate of false positive results is not surprising, because *Aspergillus* spp. can be detected in cultures of airway samples in 25% to 30% of these patients as a mere colonizer. If LT recipients were excluded, the specificity and positive predictive value in patients receiving a different SOT raised to 92.9% and 62.5%, respectively (cut-off index ≥ 1.0).

Comments. This is the first study that analyses the diagnostic contribution of GM detection in BAL in ICU patients. These findings support the usefulness of determining GM levels in BAL fluid of critically ill patients at risk for IA. The sensitivity of GM detection was 88% in proven cases when calculated on the first BAL and applying a cut-off index value of 0.5. The contribution of serum GM to the diagnosis of IA in this ICU population was much lower (sensitivity 42%). The specificity of GM detection in serum and BAL was high even in patients treated with piperacillin/tazobactam (96% and 87% respectively, cut-off index ≥ 0.5). Overall, the performance of fungal culture and/or direct examination on BAL samples was only moderate for the diagnosis of IA (sensitivity 58% for the proven cases). CT features, such as the halo sign, proved to be of no value in

ICU patients, even in the subgroup of neutropenic patients. In conclusion, the use of GM in BAL fluid as a means of establishing an early diagnosis of IA in critically ill patients at risk is very promising, and it can be a helpful instrument to decide in which circumstances antifungal therapy should be initiated early, yet the validity of these data needs to be confirmed in further studies.

Notwithstanding, as the editorialist states²³, some questions remained unanswered, such as whether we could improve serodiagnosis by more frequent sampling, test optimization, and/or by combining GM with other serum markers of aspergillosis (i.e., b-D-glucan, polymerase chain reaction, and *Aspergillus* antibodies). If we were able to optimize the diagnostic performance of serum testing, we could have an even more positive impact on aspergillosis outcome. Indeed, the repeatability of serum tests offers advantages over BAL, including earlier, easier, and more definitive diagnosis; better distinction between airway colonization and infection; prompt application of preemptive therapy; and close monitoring of response. These features will become even more valuable as the population of apparently immunocompetent hosts at risk for IPA expands even further.

Nguyen MH, Jaber R, Leather HL, Wingard JR, Staley B, Wheat LJ, et al. Use of bronchoalveolar lavage to detect galactomannan for diagnosis of pulmonary aspergillosis among nonimmunocompromised hosts. *J Clin Microbiol.* 2007;45:2787-92.²⁴

IPA is a rare disease outside patients with hematologic malignancies and those who have undergone HSCT or SOT. At present, lung biopsies are the diagnostic "gold standard" but are limited by sensitivity and complications. While the isolation of *Aspergillus* spp. from the respiratory tracts of high-risk patients is predictive of pulmonary aspergillosis, culture is limited by poor sensitivity. The objective of the present study was to assess the utility of GM detection in BAL fluid in the diagnosis of IPA in 73 nonimmunocompromised ICU patients with pulmonary infiltrates²⁴.

All patients with proven IPA (6) had a BAL GM level of >1.18 . The sensitivity, specificity, and negative predictive value (NPV) for a BAL GM level of >1.0 were 100%, 88.1%, and 100%, respectively. Notably, the positive predictive value (PPV) was only 42.9%, likely reflecting the low prevalence of pulmonary aspergillosis among nonimmunosuppressed patients. The combination of BAL microscopy and culture had a sensitivity and NPV similar to those of BAL GM detection but a higher specificity and PPV (92.5% and 54.6%, respectively). Moreover, a BAL GM test did not identify any cases that were not diagnosed by conventional methods like microscopy and culture. In conclusion, there was no conclusive benefit of determining BAL GM levels in the diagnosis of pulmonary aspergillosis among nonimmunocompromised hosts. Given the likelihood of false-positive results, a BAL GM test should not be ordered routinely in this population.

Comments. The authors present a retrospective study to assess the utility of the BAL to detect GM with only six patients with pulmonary aspergillosis. Consequently, the observations from this study should be corroborated in prospective studies. The findings differ from those of previous reports of BAL GM testing among hematologic malignancy, HSCT, and SOT patients, for whom the test generally added to the sensitivity of microscopy and culture and identified cases of pulmonary aspergillosis that were not diagnosed by these methods. The authors also suggest that the combination of BAL and serum GM might be useful in subsets of nonimmunocompromised patients for whom IPA is a serious diagnostic consideration. However, physicians should exercise restraint in ordering and interpreting BAL GM tests for nonimmunocompromised hosts in order to avoid overdiagnosing pulmonary aspergillosis and subjecting patients to unnecessary treatments.

Saito T, Shime N, Itoh K, Fujita N, Saito Y, Shinozaki M, et al. Disseminated aspergillosis following resolution of *Pneumocystis pneumonia* with sustained elevation of beta-glucan in an intensive care unit: a case report. *Infection*. 2009;37:547-50.²⁵

IA is a major cause of morbidity and mortality in immunocompromised patients receiving intensive care. The double-sandwich ELISA for galactomannan is reported to have a high sensitivity (96.5%) for the detection of invasive aspergillosis when a cut-off value of 0.8 ng/mL is used²⁶. However, the authors experienced a case of lethal disseminated aspergillosis following resolution of *Pneumocystis pneumonia* in a patient that presented with a negative galactomannan (GM) test and persistent elevation of beta-D glucan (BG) levels.

An interesting feature in this case is the dissociation of the two adjunctive fungal parameters, GM and BG. The BG, a polysaccharide component of fungal cell walls, is an adjunctive parameter suggesting possible deep mycosis, but is nonspecific with respect to fungal infections. Thus, this case suggests that persistent elevated BG levels (>100 pg/mL) in spite of clinical and pathological improvement of *Pneumocystis pneumonia*, refractory to trimethoprim-sulfamethoxazole and fluconazole, may suggest possible *Aspergillus* infection and should prompt the initiation of empiric anti-aspergillosis therapies in patients at risk for fungal infection.

Kralt D, Light B, Cheang M, MacNair T, Wiebe L, Limerick B, et al. Clinical characteristics and outcomes in patients with pulmonary blastomycosis. *Mycopathologia*. 2009;167:115-24.²⁷

Blastomycosis is an uncommon granulomatous infection caused by the thermally dimorphic fungus *Blastomyces dermatitidis*. The most frequent clinical infections involve the lung, skin, and bone. Pulmonary manifestations range from asymptomatic self-limited infection to severe diffuse pneumonia causing respiratory failure. The objective of this study is to establish the clinical characteristics and outcomes of patients with pulmonary blastomycosis diagnosed at hospitals in Manitoba and northwestern Ontario, Canada. This was a retrospective review of medical records of 318 patients with blastomycosis in these regions. The majority of patients were Caucasian (198 [62.5%] patients), male (193 [61%] patients), and residents of Ontario (209 [65.7%] patients). Most patients were treated in an inpatient hospital ward (266 [84%] patients) and survived (294 [92%] patients). Pulmonary involvement, either alone or associated with other sites, was present in 296 (93%) of the 318 patients; 22 (7%) patients had no evidence of pulmonary blastomycosis. The majority of patients had localized lung disease (1-3 quadrants on chest radiograph involved; 225 (82%) patients). Of 294 (92%) patients requiring hospitalization, 266 (90%) patients received all inpatient care on a general medical ward; 28 (10%) patients required admission to the ICU. Factors associated with ICU admission included diffuse pulmonary disease (four quadrants involved on chest radiograph), diabetes, and prior use of antimicrobial therapy. Twenty-four (8%) patients died, and multivariate analysis showed that older age and Aboriginal ethnicity were the significant risk factors for death from blastomycosis.

Comments. Blastomycosis is a cause of serious, potentially life-threatening pulmonary infection in this geographic region. This entity should be considered in the differential diagnosis of patients with a severe LRT infection and with a history of previous travel to known areas of endemicity for the disease.

Schaffer K, Fitzgerald SF, Commene M, Maguiness A, Fenelon LE. A pseudo-outbreak of *Fusarium solani* in an intensive care unit associated with bronchoscopy. *J Hosp Infect*. 2008;69:400-2.²⁸

BAL is a frequently used diagnostic procedure in ICUs to evaluate

patients with respiratory problems. Among medical instruments, endoscopes are commonly implicated in nosocomial outbreaks. In June 2006 the hospital infection control team of this hospital noticed that a number of BAL samples from ICU patients had grown *Fusarium solani*. An epidemiological investigation was carried out to define the extent and the source of this cluster and to institute control measures. All of the patients had undergone bronchoscopy with a direct vision bronchoscope (BF type 20D, OLYMPUS) only used in the ICU. Although the bronchoscope could not be confirmed as the source of the contamination by microbiological culturing, circumstantial evidence was felt to be strong enough to permanently remove the bronchoscope from use. All of the patients had been investigated using the same instrument, no other lavage performed in the hospital grew *F. solani* and the pseudo-outbreak stopped after the bronchoscope had been removed from service. Cultures from the internal channels of the bronchoscope, from air sampling from the ICU and from water samples from the hospital main water tanks and the ICU department were negative for *F. solani*. The origin of contamination of the bronchoscope that led to the cluster of cases could not be established.

This publication illustrates a nosocomial mould outbreak not related to airborne contamination.

Conflict of interest

The authors declare they have not any conflict of interest.

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