Commentary

A validated clinical approach for the management of aspergillosis in critically ill patients: ready, steady, go!

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See related research by Vandewoude *et al*. in issue 10.1 [http://ccforum.com/content/10/1/R31]

Abstract

The clinical relevance of recovering *Aspergillus* species in intensive care unit patients is unknown. Diagnosis of invasive pulmonary aspergillosis is extremely difficult because there are no specific tests sensitive enough to detect it. The rapidly fatal prognosis of this infection without treatment justifies early antifungal therapy. A clinical algorithm may aid clinicians to manage critically ill patients from whose respiratory specimens *Aspergillus* spp. have been isolated. This new tool needs to be validated in a large cohort of patients before it can be recommended.

The management of critically ill patients with a suspected invasive fungal infection based on predefined clinical and microbiological criteria or the punctuation of a score may be a valid approach when the definitive diagnosis is feasible only in a small proportion of patients. This is what Vandewoude and colleagues propose with their retrospective analysis of all patients who had *Aspergillus* spp. isolated from their respiratory samples [1].

Fungal infections have increased in intensive care units (ICUs) over the past decades. Although less common than candidiasis, aspergillosis is more likely to result in a life-threatening infection. The most important host defences against *Aspergillus* are neutrophils and alveolar macrophages. Thus, neutropenic patients, and those who receive long-lasting corticosteroid treatments, are at high risk for invasive aspergillosis [2].

Exposure to *Aspergillus* spp. is a common occurrence. This organism grows on a wide variety of organic material and the conidia are easily aerosolised. Although exposure is universal, invasive infection occurs almost entirely in immunosuppressed individuals. Outbreaks have been described in bone marrow transplantation, solid organ transplant recipients and leukaemia patients in association with hospital construction and/or ventilation system contamination with *Aspergillus*. Moreover, hospital water is a frequently overlooked source of nosocomial aspergillosis [3].

Critically ill patients can also develop invasive aspergillosis independent of classic risk factors [4,5]. Indeed, multiple organ failure and prolonged stays in the ICU are associated with a complex decrease in immune functions, deactivation of macrophages and altered cellular response [6].

Diagnosis of invasive aspergillosis with confidence is extremely difficult in ICU patients. Isolation of *Aspergillus* spp. may correspond to a mere colonisation. Confirmation of the diagnosis obliges the demonstration of histopathological evidence of *Aspergillus*. This is usually not feasible given the special circumstances of critically ill ventilated patients. Likewise, screening the blood for galactomannan may be very valuable in neutropenic patients but its usefulness in ICU patients is limited. Before new antifungal agents were available, mortality of critically ill patients with invasive aspergillosis was nearly 100% [7,8]. Currently, the therapeutic armoury has significantly improved with the introduction of new azoles (i.e., voriconazole) and the echinocandins (i.e., caspofungin), a new class of drugs with a novel target [9,10].

Many problems contribute to the lack of confident and timely diagnosis of invasive aspergillosis in critically ill patients. On one hand, the early administration of antifungal agents may be life-saving, but clinicians must also bear in mind the problems and costs associated with needless treatments derived from the overinterpretation of the potential clinical significance of isolates of *Aspergillus* spp. in respiratory samples. How can we attempt to solve this dilemma?

ICU = intensive care unit.

Van de Woude *et al*. [1] propose a clinical algorithm based on the criteria defined by an international conference on the diagnosis of aspergillosis in immunocompromised patients [11]. With this approach, approximately 50% of the patients were diagnosed with invasive aspergillosis and in the other 50% the isolation was considered colonization [1]. These diagnoses were confirmed in all cases in which histology was obtained. Unfortunately, histology was available only in a small proportion of patients (one-fourth of patients with presumed diagnosis of infection and one-tenth of the patients with the diagnosis of colonization). At first glance, these results seem very hopeful, although positive and negative predictive values cannot be calculated with these figures.

The diagnostic accuracy of this algorithm can be improved. Many authors have documented that invasive aspergillosis can occur in certain types of 'non-immunocompromised' critically ill patients. Three high risk groups stand out for invasive aspergillosis: chronic obstructive pulmonary disease [4,5], prolonged multiple dysfunction syndrome in the situation of immunoparalysis [12], and severe hepatic failure [4]. These underlying conditions are not included in the proposed criteria and they should be added to the list. This may avoid the misclassification of these high risk patients if semiquantitative culture of bronchoalveolar lavage was not positive [13], a criterion not universally accepted. Moreover, a high resolution CT scan is nowadays mandatory and a normal portable chest X-ray may lead to an erroneous classification [2].

The significance of a positive respiratory culture for *Aspergillus* spp. in a non-immunodepressed patient causes the clinician great uncertainty and doubt. Nowadays, the isolation of *Aspergillus* spp. in a critically ill patient is not an exceptional curiosity. Definitions proposed by the European Organisation for the Research and Treatment of Cancer were not designed to guide clinical practice [11]. Critical care physicians need a helpful instrument to decide in which circumstances antifungal therapy should be initiated early, given the high mortality of this infection but the availability of new and active agents. Obviously, this and other strategies need to be validated in large cohorts of critically ill patients before they can be recommended [13,14]. This is an urgent task because we do not expect to have at our disposal a precise microbiological test in the near future. Therefore, ready, steady, go!

Competing interests

The authors declare that they have no competing interests.

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