

Scientific Letter

Aspergillus* Pneumonia in an Immunocompetent Patient**Neumonía por *Aspergillus* en un paciente inmunocompetente***

Dear Editor,

Our patient was a 55-year-old woman, non-smoker, diagnosed with bronchiectasis associated with Swyer–James–MacLeod syndrome, involving severe airflow obstruction. She had no prior respiratory comorbidities or any other comorbidities and no exacerbations in recent years. She was receiving β -agonist bronchodilators, muscarinic antagonists and inhaled corticosteroids at medium doses, without azithromycin or inhaled antibiotics.

She attended the emergency department for a 10-day history of cough with yellowish expectoration, fever and dyspnea, that did not respond to oral levofloxacin for 5 days. She denied symptoms of viral infection in the previous weeks. She had 12,300 leukocytes/ μ L (with 67.3% neutrophils) and a procalcitonin level of 0.01 ng/mL. Respiratory viral detection tests were negative for SARS-CoV-2, respiratory syncytial virus and influenza A and B using nasal exudate polymerase chain reaction. In addition, urine pneumococcal and *Legionella* antigens, sputum auramine stain and blood cultures were negative. Chest X-ray showed ill-defined and patchy nodular opacities in the right upper lobe and right base, bilateral apical pleural thickening and hyperclarity in the left hemithorax (Fig. 1a). Treatment with piperacillin–tazobactam began. However, she presented progressive worsening, with daily fever, brownish expectoration, dyspnea at rest, and basal oxygen saturations of 89%. After 4 days, piperacillin–tazobactam was replaced by intravenous meropenem and cotrimoxazole. However, 2 days later, the patient continued to deteriorate, with a baseline saturation of 87%, increasing dyspnea and sputum purulence. Six days after admission, a sputum culture revealed substantial growth of *Aspergillus fumigatus* complex and *Aspergillus flavus*, along with the usual bacterial microbiota. Furthermore, on the sixth day of admission, a CT scan of the chest showed marked deterioration, with extensive parenchymal opacities in all pulmonary lobes of the right hemithorax and patchy opacities in the left upper lobe (Fig. 2a and b). Given the suspicion of *Aspergillus* pneumonia and the high mortality associated with delayed treatment,¹ antibiotics were suspended and treatment with oral voriconazole began on the same day. From 72 h onwards, the patient remained afebrile, with decreased dyspnea and sputum volume and purulence, and baseline saturations of 90%. Five days after starting antifungal therapy, the patient was discharged from the hospital with oxygen at 1 lpm and oral voriconazole. At 3 weeks, expectoration and dyspnea had resolved and her baseline saturation was 95%. Voriconazole was maintained for a total of 6 weeks. Chest X-ray 3 months after onset of the treatment showed complete resolution of right upper lobe and base opacities (Fig. 1b). During

the following 15 months, the patient did not present any further exacerbations.

Aspergillus spp. is a filamentous fungus that can cause numerous pathologies. The most frequently isolated species is *A. fumigatus*. The spores of the fungus are usually cleared from the airways and do not cause disease, but rather simple colonization or contamination, especially outside the setting of a critical illness and in the absence of immunosuppression.² Our patient had a heavy growth of *Aspergillus* in the sputum sample, and this, in the setting of rapidly progressive pneumonia, is, in our opinion, fairly confirmatory evidence of *Aspergillus* pneumonia. Other tests such as galactomannan (in plasma/serum or bronchoalveolar lavage) or serum beta-D-glucan were not performed because their role in *Aspergillus* pneumonia (and in other entities such as invasive aspergillosis in the immunocompetent host, *Aspergillus* bronchitis or chronic necrotizing pulmonary aspergillosis) has not been established. Its susceptibility depends on the immune status of the host. Patients with hematological malignancy (associated with neutropenia, for example) are more sensitive than those without risk factors.³ Fiberoptic bronchoscopy was not performed because tissue invasion by fungal hyphae in the early stages of *Aspergillus* pneumonia has not been demonstrated.

The imaging characteristics of *Aspergillus* pneumonia are non-specific and indistinguishable from those of other types of pneumonia. Initial chest radiographs typically reveal localized infiltrates, and if adequate antifungal treatment is not initiated, these localized infiltrates progress to become diffuse and bilateral infiltrates,^{1,4} as evidenced by the CT scan of the patient in this case. Classic radiological findings, such as the halo sign and the air crescent sign, are associated with invasive pulmonary aspergillosis. The halo sign is defined as an area of low attenuation surrounding a pulmonary nodule, while the air crescent sign develops later, usually during recovery of the neutrophil count. The air crescent sign has been observed in approximately 50% of patients with invasive pulmonary aspergillosis; however, it has not been commonly described in patients with *Aspergillus* pneumonia^{3,5} (Fig. 2a and b).

The optimal duration of antifungal therapy for patients with *Aspergillus* pneumonia has not been the subject of study. The recommended duration of therapy for invasive *Aspergillus* diseases in non-neutropenic intensive care unit patients is from 6 to 12 weeks, depending on disease severity and the efficacy of treatment and infection clearance.⁶ However, given the favorable progression of our patient and the less severe nature of her *Aspergillus* pneumonia, we elected to discontinue treatment after 6 weeks. The likelihood of the patient experiencing spontaneous resolution (or coincidentally receiving with treatment with voriconazole) or of the underlying cause being unrelated to a fungal infection is considered to be low. The possibility of bacterial etiology can be excluded on the basis of an absence of response to antibiotics and the absence of bacterial organisms identified in the sputum culture. The most prevalent

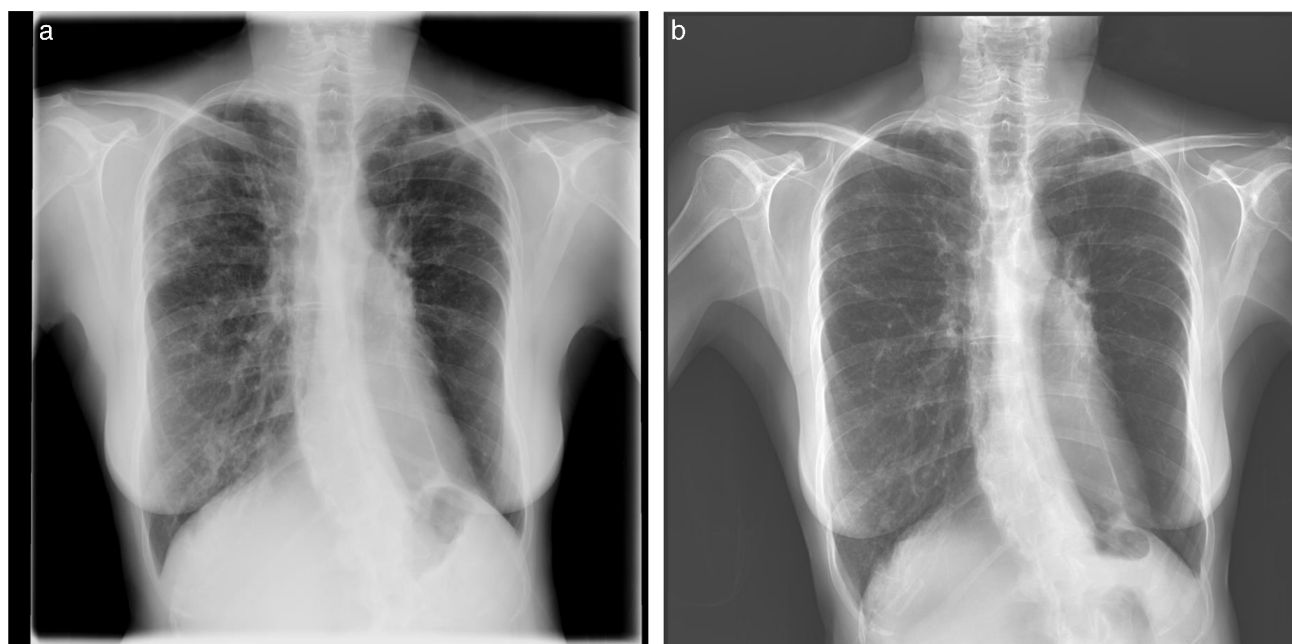


Fig. 1. (a) Chest X-ray showing ill-defined and patchy nodular opacities in the right upper lobe and right base, bilateral apical pleural thickening, and hyperclarity in the left hemithorax. (b) Chest X-ray 3 months after onset of treatment showing complete resolution of right upper lobar and basal opacities.

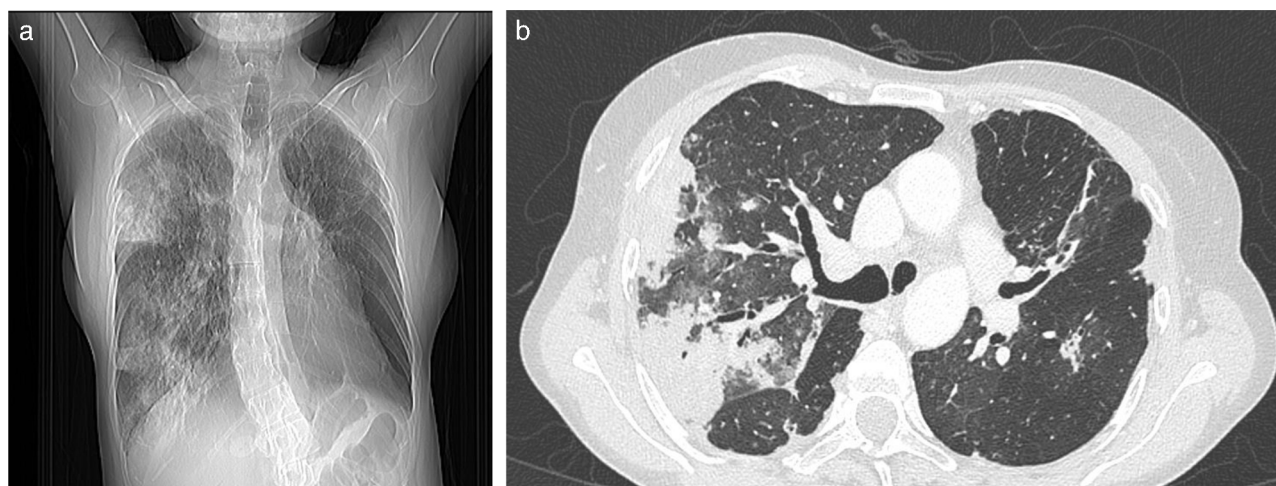


Fig. 2. (a) Computed coronal tomography of the chest showing extensive parenchymal opacities in all pulmonary lobes of the right hemithorax. (b) Computed axial tomography of the chest showing extensive parenchymal opacities in all pulmonary lobes of the right hemithorax and patchy opacities in the left upper lobe.

viruses associated with the presence of radiological infiltrates are SARS-CoV-2 and influenza, and both of these were excluded based on pharyngeal exudates. The likelihood of organizing pneumonia is also low, as the patient was not treated with oral corticosteroids.

Aspergillus pneumonia has been exceptionally reported in immunocompetent patients,^{1,2} and indeed, most reviews do not mention this entity.^{7,8} Three features are usually required: marked exposure to fungal spores, previous viral infection, and chronic lung disease, usually emphysema or chronic obstructive pulmonary disease.² The distinguishing feature of this case report is that, despite the patient's only underlying risk factor being a chronic obstructive pulmonary condition, an early diagnosis of *Aspergillus* pneumonia was made and the patient began antifungal treatment promptly and expeditiously. Clinicians must be aware of the risk of *Aspergillus* pneumonia and other forms of aspergillosis in patients with chronic respiratory diseases, in order to facilitate early diagnosis and management. A delay in diagnosis and the absence of

antifungal therapy are associated with a poor prognosis and/or progressive disease.² A suboptimal clinical and radiological response to antibiotic treatment should give rise to the consideration of entities such as *Aspergillus* pneumonia in patients with chronic lung disease.

Informed Consent

We obtained the patient's informed consent to publish her case.

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Authors' Contributions

All authors have contributed to the preparation, review and writing of the article.

Conflicts of Interest

The authors declare that they have no conflict of interest in relation to the subject matter.

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Luis Máiz *, Rosa Nieto, Edwin Yong

Chronic Bronchial Infection Unit, Pneumology Department, Ramón y Cajal Hospital, Alcalá de Henares University, Madrid, Spain

* Corresponding author.

E-mail address: luis.maiz@salud.madrid.org (L. Máiz).