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Abstract (publication only)

**Aspergillus lentulus is a marker of poor prognosis in non-haematologic patients with invasive pulmonary aspergillosis**

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Background: *Aspergillus lentulus*, which can be morphologically misidentified as *A. fumigatus*, has occasionally been reported to cause invasive aspergillosis (IA). Its epidemiology is mostly unknown. We report 7 patients (pts) with IA caused by *A. lentulus* who were admitted to a tertiary hospital in Madrid, Spain from November 1999 to July 2012. Methods: Morphologically identified *A. fumigatus* isolates from 174 pts with proven/probable IA underwent beta-tubulin sequencing. Seven pts (57% male, median age 61 years) had probable pulmonary IA caused by *A. lentulus* (n=20 isolates). Antifungal susceptibility was obtained using the CLSI M38-A2 method. Results: The predisposing conditions were corticosteroid use (100%), autoimmune disease (57%), solid tumor (43%), chronic liver disease (43%), chronic obstructive pulmonary disease (28.6%), haematologic neoplasm (14.3%), and other (14.3%). Most pts (71.4%) presented with dyspnea. Cough and fever were common (57% and 43%). Nonspecific radiological findings such as infiltrates (85.7%) and pleural effusion (57.1%) were present, as were pulmonary nodules (42.9%) and cavitations (14.3%). *A. lentulus* was isolated from sputum (5 pts), sputum plus bronchoalveolar lavage (BAL) (1 pt), and BAL (1 pt). In 3 pts, *A. lentulus* was the only species found, but 4 pts were co-infected with other molds (other *A. fumigatus* complex, n=4; *A. terreus* complex, n=3; *A. flavus*, n=1; *Aspergillus* spp., n=2; *Cunninghamella* spp., n=1). The median *Aspergillus* score in the 7 cases was 3 points. Serum galactomannan determinations were positive in 5/6 (83.3%) pts. All pts received antifungal agents as monotherapy (n=4) or in combination (n=3); 5 pts received sequential therapy. The antifungal agents used were voriconazole (n=6), liposomal amphotericin B (n=4), caspofungin (n=4), terbinafine (n=2), posaconazole (n=1), anidulafungin (n=1), and micafungin (n=1). Most pts (6/7) had a poor prognosis. Six pts were diagnosed after 2009. The antifungal susceptibility of the isolates (MIC<sub>90</sub>/MIC range) for itraconazole, voriconazole, and posaconazole was 2/1-2 µg/ml, 4/1-4 µg/ml, and 1/0.25-1 µg/ml. Conclusion: Most patients with invasive aspergillosis caused by *A. lentulus* had non-haematologic predisposing conditions and high mortality (85%). *A. lentulus* was commonly found as a copathogen with other *Aspergillus* spp. *A. lentulus*, which shows reduced susceptibility to azoles, seems to have emerged since 2009.