

# Fatal invasive pulmonary aspergillosis due to *Aspergillus pseudodeflectus* in a liver transplant patient: first case report

Nawel AIT-AMMAR<sup>1,2</sup>, Eric LEVESQUE<sup>3</sup>, Jean-Benjamin MURAT<sup>2</sup>, Françoise FOULET<sup>2</sup>, Eric DANNAOUI<sup>2,4</sup>, Jean-Claude MERLE<sup>3</sup>, Françoise BOTTEREL<sup>1,2</sup>

<sup>1</sup>Unité de Parasitologie-Mycologie, CHU Henri Mondor, APHP, 94010 Créteil, France  
<sup>2</sup>EADynamyc, UPEC, ENVA, Faculté de Médecine de Créteil, 94010 Créteil, France  
<sup>3</sup>Service d'Anesthésie-Réanimation, CHU Henri Mondor, APHP, 94010 Créteil, France  
<sup>4</sup>Unité de Parasitologie-Mycologie, HEGP, APHP, 75015 Paris, France

EV0769

## Introduction

- Liver transplant recipients are a population at risk for developing invasive aspergillosis
- Aspergillus fumigatus* is the most common species but other non-*fumigatus* *Aspergillus* species, in particular can be involved with reduced sensitivity to antifungal drugs
- We report a case of invasive pulmonary aspergillosis due to *Aspergillus pseudodeflectus* in a liver transplant recipient
- To our knowledge, we describe the first reported case of invasive aspergillosis due to *A. pseudodeflectus*

## Molecular identification

Sequencing of a partial  $\beta$ -tubulin and calmodulin genes was performed. A BLAST search in GeneBank and MycoBank revealed *A. pseudodeflectus* as an identification. This species belongs to *Aspergillus* section *Usti* and is very close to *Aspergillus calidoustus*<sup>2</sup> previously reported in human pathology.

### Calmodulin sequence of the isolate

CCGAGTACAAGGARGCCTTCTCCCTATTGTAAGTCGCCACGAAATCTATAACTGATCGCTATCTAAGAATCCCTTATTACCCTTTTCGGCTTGAACAGGACAAGGATGGTATGGTTAGTGAACCCACCCACTCCGGCAACGTTATCGCATACGCTCAGCCTCGATTATCCATAATGTTAGCCCATCAATTAGCCTGTATTGATAATGTGTGAATGCGTTTAGGCCAGATACCACCAAGGAACTCGGCACTGTGATGCGCTCGCTCCGGCAGAACCCCTCCGAGTCTGAACCTCCAGGACATGATCAACGAGGTTGACGCCGACAACAACGGCACCATTGATTTCCAGGTATATACTACGATACAACCTCTAGGCTTACAGGATATTGGCAGATCACTACTCAAAAAATATATACAGATTCTCCACAATGATGGCCAGAAAGATGAAGGACACCGACTCCGAGGAGAAATCCGAGAGGCTTCAAGGTTTCGACCGTGACAACAATGGTTTCTCAGCTGCCAAGTCCGCCACGTRATGACCTCRATCGGB

Description	Max score	Total score	Query cover	E value	Ident	Accession
<a href="#">Aspergillus pseudodeflectus strain AS3_15309 calmodulin (cmd) gene, partial cds</a>	983	983	100%	0.0	100%	JN692677.1
<a href="#">Aspergillus pseudodeflectus strain AS3_15308 calmodulin (cmd) gene, partial cds</a>	983	983	100%	0.0	100%	JN692679.1
<a href="#">Aspergillus pseudodeflectus isolate NRRL_278 calmodulin gene, partial cds</a>	983	983	100%	0.0	100%	EF652368.1
<a href="#">Aspergillus pseudodeflectus isolate NRRL_6135 calmodulin gene, partial cds</a>	977	977	100%	0.0	99%	EF652419.1
<a href="#">Aspergillus calidoustus partial calM gene for calmodulin, strain E188M09</a>	966	966	100%	0.0	99%	H5931690.1
<a href="#">Aspergillus calidoustus partial calM gene for calmodulin, strain Kw18-12014</a>	966	966	100%	0.0	99%	H5931699.1
<a href="#">Aspergillus calidoustus strain AS3_15302 calmodulin (cmd) gene, partial cds</a>	966	966	100%	0.0	99%	JN692676.1
<a href="#">Aspergillus calidoustus partial calM gene for calmodulin, strain CBS 121601, exons 1-4</a>	966	966	100%	0.0	99%	HE186559.1

BLAST.ncbi.nlm.nih.gov/calmodulin/sequence

## Case report

- In May 2013, a 64-year-old woman with drug-induced fulminant hepatitis underwent liver transplantation
- Prophylactic treatment with caspofungin was introduced due to aspergillosis risk factors consisting in hemodialysis and fulminant hepatitis<sup>1</sup>
- Six weeks after transplantation, CT scan showed a right pulmonary opacity. At the same time, an increase of galactomannan and  $\beta$ -D-glucan was observed with a positive *Aspergillus* PCR in blood (CT=35)

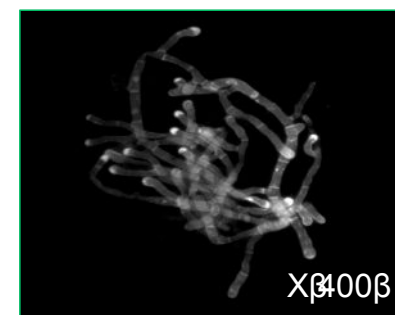
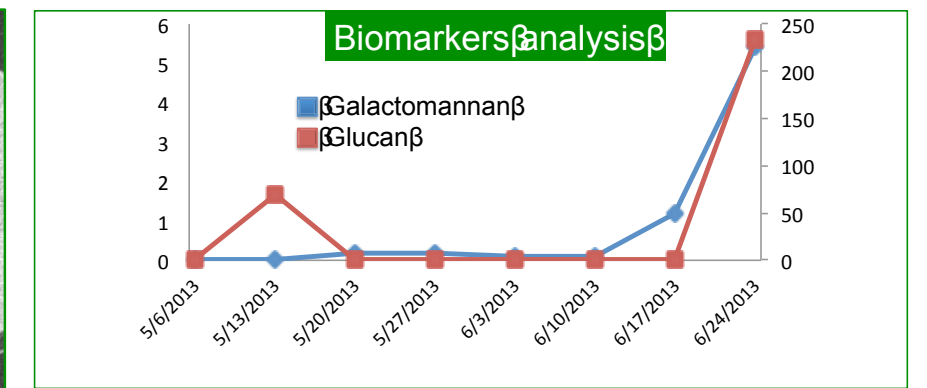


Fig. 1 Direct examination of BAL (calcofluor)



Fig. 2 Macroscopic aspect of BAL culture

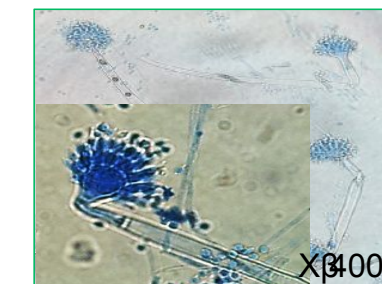
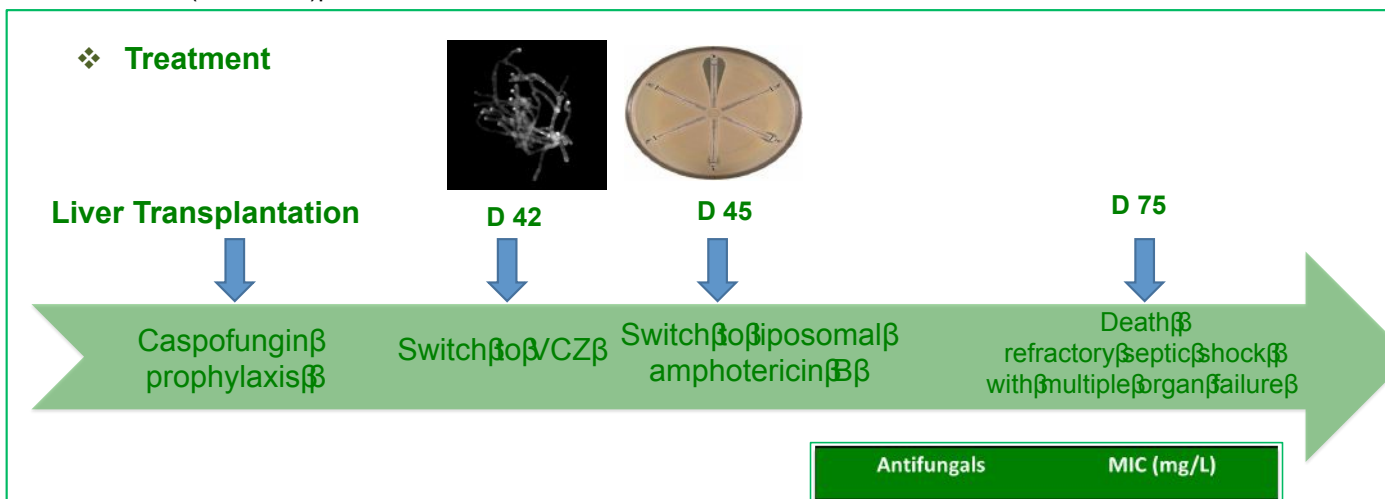


Fig. 3 Microscopic aspect of colonies

- Direct examination of BAL showed *Aspergillus*-like branching hyphae (fig. 1)
- Culture of BAL at 37°C grew with several colonies of a white to brown filamentous fungus with a velvety appearance (fig. 2)
- Microscopic examination of the colonies showed *Aspergillus* biserial conidial heads with curved conidiophores (fig. 3)
- Patient classified in probable invasive aspergillosis (EORTC/MSG Criteria)
- After several infections (*S. maltophilia* pneumopathy, *E. coli* and *E. faecium* abdominal infections) and hemorrhagic complications, the patient died



- The antifungal susceptibility tests (E-test®) of this *Aspergillus* sp. revealed low MICs for echinocandins but high MICs to azoles, as described in the literature

Antifungals	MIC (mg/L)
Amphotericin B	0.75
Itraconazole	12
Voriconazole	4
Posaconazole	6
Micafungin	0.016
Caspofungin	0.5

## Conclusion

- Our case reports an invasive pulmonary aspergillosis in a liver transplant recipient due to a species newly described in human pathology: *A. pseudodeflectus*. This species has lowered susceptibility to azoles.
- Accurate identification associated to antifungal susceptibility testing is essential for therapy adjustment.

## References

- Gavaldà B. et al., Clin Microb Infect, 2014
- Samson RA. et al., Stud Mycol, 2011

Contact: francoise.botterel@aphp.fr