Rare invasive mold infections in Greece; registry and analysis of cases from January 2014 - December 2017

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OBJECTIVES

National registries are important and necessary for the study and monitoring of rare invasive mold infections.

Our group has started a multicentre registry in Greece since 2005, along with the ECMM/ISHAM Global Registry initiative for zygomycosis (mucormycosis) (www.zygomyco.net).

The aim of the present study was:

- to determine the epidemiology of serious rare mold infections in Greece during the years 2014-2017, and the organisms involved
- to analyze any associations between the isolated fungi and clinical presentation, underlying diseases, risk factors and outcome

Table: Distribution of cases according to infectious agents

Organism	N	Isolation site	underlying conditions
Mucorales	16		
<i>Rhizopus arrhizus</i>	9	6 sinus, 1 dissemin. (knee/lung), 1 lung, 1 urine	3 haematologic malignancy, 1 DM*, 2 SO Ca/DM, 1 MDS, 1 IgA nephropathy/steroid-related DM, 1 ureterostomia
<i>Lichtheimia</i> spp.	2	soft tissue/skin,	1 burns, 1 traffic accident
<i>Mucor</i> spp.	1	bronchial /gastric secretions,	*Child with hydrocephalus and shunt, after intubation following status epilepticus.
unidentified genus	1	brain tissue	traffic accident
no growth	3	1 sinus, 1 lung, 1 skin	1 DM, 1 Ca, 1 flooding victim
Fusarium	13		
<i>F. proliferatum</i>	1	cornea	eye injury
<i>F. solani</i>	1	blood	haematol. malignancy
<i>F. dimerum</i>	1	blood	haematol. malignancy
<i>Fusarium</i> spp.	10	4 cornea, 4 blood, 2 skin	4 keratitis (1 eye injury, 1 contact lens, 1 after herpes infection, 1?), 2 ARDS, 1 brain injury, 1 HSCT, 2 leg injury
<i>Purpureocillium lilacinum</i>	2	keratitis	eye injury
<i>Scedosporium apiospermum</i> SC	1	bronchial secretions,	HSCT
<i>Alternaria</i> spp.	2	keratitis	1 contact lens, 1?
<i>Bipolaris</i> spp.	1	BAL	AML relapse, neutropenia

* possible, DM diabetes mellitus, SO: solid organ, Ca: cancer, MDS: myelodysplastic syndrome, ARDS: acute respiratory distress syndrome, HSCT: haematopoietic stem cell transplantation, AML: acute myeloid leukemia

RESULTS

New cases number (N): 35, of which 16 due to *Mucorales*, 13 due to *Fusarium*, and 6 due to other rare molds: *Purpureocillium lilacinum* (2), *Scedosporium apiospermum* species complex (SC) (1), *Alternaria* (2) and *Bipolaris* (1) (**Table**). **The frequency of cases was 8.7/year, comparable to that of previous years.**

Mucorales (14 proven, 2 possible, EORTC/MSG criteria). Most cases with *Rhizopus arrhizus* were from patients with rhino-orbito-cerebral mucormycosis. More frequent underlying conditions: hematologic malignancy, diabetes mellitus (DM) and soft tissues/skin after serious injuries following accidents (**Fig. 1 a, b**).

The 2 *Lichtheimia* species were isolated from soft tissues from patients with severe trauma after road accidents.

*Case Fatality Rate for mucormycosis: 50%.

The ***Fusarium*** strains were isolated from blood cultures of severely ill patients, and from corneal or skin ulcers of immunocompetent, after trauma (**Table** and **Fig. 2 a, b**).

Fig. 1

Fig. 2

MATERIALS AND METHODS

Prospective, observational, non-interventional, nationwide clinical and laboratory study (ongoing).

Patient material, data and available strains were sent to our laboratory for laboratory diagnosis, recording, fungal identification and antifungal susceptibility testing whenever needed (EUCAST broth microdilution methodology).

In cases with no fungal growth, formalin fixed and paraffin embedded (FFPE) tissues were collected for histopathological and molecular analysis.

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CONCLUSIONS

- ✓ Rare invasive mold infections remain rare in our region.
- ✓ More prominent are: mucormycosis in patients with haematologic malignancies, diabetes and trauma, and fusariosis in keratitis cases and severely ill patients.
- ✓ Ocular trauma and soft contact lens use are also important risk factors for keratitis due to other rare molds.

REFERENCES

1. Skiada A, Pagano L, Groll A, et al.: Zygomycosis in Europe: analysis of 230 cases accrued by the registry of the European Confederation of Medical Mycology (ECMM) Working Group on Zygomycosis between 2005 and 2007. *Clin Microbiol Infect*. 2011; **17**: 1859–67.
2. Tortorano, A.M. et al. Confederation of Medical Mycology (ECMM) epidemiological survey on invasive infections due to *Fusarium* species in Europe. *Eur J Clin Microbiol Infect Dis* 2014; **33**: 1623–1630.
3. Skiada A, Pavleas I, Drogari-Apiranthitou M. Rare fungal infectious agents: a lurking enemy. *F1000Res*. 2017; **6**:1917.