

Coronavirus Disease 2019-Associated Mucormycosis in France: A Rare but Deadly Complication

François Danion, Valérie Letscher-Bru, Juliette Guitard, Karine Sitbon, Sarah Dellière, Adela Angoulvant, Guillaume Desoubeaux, Françoise Botterel, Anne-Pauline Bellanger, Gilles Gargala, et al.

▶ **To cite this version:**

François Danion, Valérie Letscher-Bru, Juliette Guitard, Karine Sitbon, Sarah Dellière, et al.. Coronavirus Disease 2019-Associated Mucormycosis in France: A Rare but Deadly Complication. Open Forum Infectious Diseases, 2022, 9 (2), pp.180-190. 10.1093/ofid/ofab566 . hal-03962472

HAL Id: hal-03962472

https://hal.sorbonne-universite.fr/hal-03962472

Submitted on 9 Feb 2023

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



Distributed under a Creative Commons Attribution - NonCommercial - NoDerivatives 4.0 International License

Open Forum Infectious Diseases

BRIEF REPORT

Coronavirus Disease 2019-Associated Mucormycosis in France: A Rare but Deadly Complication

François Danion,[1,2] Valérie Letscher-Bru,[3] Juliette Guitard,[4] Karine Sitbon,[5] Sarah Dellière,[6] Adela Angoulvant,[7,8] Guillaume Desoubeaux,[9] Francoise Botterel,[10] Anne-Pauline Bellanger,[11] Gilles Gargala,[12] Fabrice Uhel,[13] Marie-Elisabeth Bougnoux,[14] Victor Gerber,[15] Justin Michel,[16] Marjorie Cornu,[17,18] Stéphane Bretagne,[5,6] Fanny Lanternier[5,19]; and the COVID-Mucor study group

[1]Université de Strasbourg, Hôpitaux Universitaires de Strasbourg, Service de Maladies Infectieuses et Tropicales, Strasbourg, France, [2]Laboratoire d'ImmunoRhumatologie Moléculaire, INSERM Unité Mixte de Recherche_S 1109, Strasbourg, France, [3]Université de Strasbourg, Hôpitaux Universitaires de Strasbourg, Laboratoire de Mycologie-Parasitologie, Strasbourg, France, [4]Sorbonne Université, Inserm, Centre de Recherche Saint-Antoine, CRSA, Assistance Publique-Hôpitaux de Paris, Hôpital Saint-Antoine, Service de Parasitologie-Mycologie, Paris, France, [5]Institut Pasteur, CNRS, Université de Paris, Unité de Mycologie Moléculaire, Centre National de Référence Mycoses Invasives et des Antifongiques, Paris, France, [6]Assistance Publique-Hôpitaux de Paris, Groupe Hospitalier Saint-Louis-Lariboisière-Fernand-Widal, Laboratoire de Mycologie-Parasitologie, Paris, France, [7]Université Paris Saclay, Assistance Publique-Hôpitaux de Paris, Hôpital Bicêtre, Service des Maladies Infectieuses et Tropicales, Le Kremlin-Bicêtre, France, [8]Institut National de Recherche pour l'Agriculture, l'Alimentation et l'Environnement, Centre National de Recherche Scientifique, AgroParisTech, GQE-Le Moulon, Gif-sur-Yvette, France, [9]Centre Hospitalier Universitaire de Tours, Laboratoire de Mycologie-Parasitologie, Tours, France, [10]Assistance Publique-Hôpitaux de Paris, CHU Henri-Mondor, Laboratoire de Mycologie-Parasitologie, Créteil, France, [11]CHU de Besançon, Laboratoire de Mycologie-Parasitologie, Besançon, France, [12]CHU de Rouen, Laboratoire de Mycologie-Parasitologie, Rouen, France, [13]Assistance Publique-Hôpitaux de Paris, Hôpital Louis-Mourier, Service de Médecine Intensive et Réanimation, Département Médical Universitaire ESPRIT, Colombes, France, [14]Université de Paris, Assistance Publique-Hôpitaux de Paris, Hôpital Necker-Enfants Malades, Laboratoire de Mycologie-Parasitologie, Paris, France, [15]Hôpitaux Civils de Colmar, Service de Réanimation Médicale, Colmar, France, [16]Université Aix Marseille, AP-HM, Hôpital de La Conception, Service Oto-Rhino-Laryngologie et Chirurgie Cervico-faciale, Marseille, France, [17]Université de Lille, Inserm U1285, CHU Lille, Laboratoire Parasitologie-Mycologie, [18]CNRS, UMR 8576 - UGSF - Unité de Glycobiologie Structurale et Fonctionnelle, Lille, France, [19]Université de Paris, Assistance Publique-Hôpitaux de Paris, Hôpital Necker-Enfants Malades, Service de Maladies Infectieuses et Tropicales, Paris, France

We studied COVID-19 associated mucormycosis based on 17 cases reported nationwide and assessed the differences with India. They differed by frequencies of diabetes mellitus (47% in France versus up to 95% in India), hematological malignancies (35% versus 1%), anatomical sites (12% versus >80% rhino-orbito-cerebral) and prognosis (88% mortality versus <50%).

Keywords. CAM; CAPA; COVID-19; mucormycosis.

Coronavirus disease 2019 (COVID-19) has a wide spectrum of severity. Fungal superinfections, notably aspergillosis, can complicate the course of severe COVID-19 with a high mortality [1]. Emerging reports, mainly from India, recently described COVID-19-associated mucormycosis (CAM). In this country, more than 28 000 cases have already been reported and mucormycosis is now a notifiable disease [2]. Outside India, only a few case reports have been published [3, 4]. The aim of our study was to describe cases of CAM in France and analyze host factors, presentation, and outcome.

METHODS

We conducted a retrospective nationwide study on CAM. Our network of 59 French mycology laboratories, which covers most of the French territory, was requested to report CAM cases diagnosed from March 2020 to June 10, 2021 to the French National Reference Center for Invasive Mycosis and Antifungals (NRCMA) as part of its surveillance missions. Only cases occurring within the 3 months after COVID-19 diagnosis confirmed by a positive polymerase chain reaction (PCR) for severe acute respiratory syndrome coronavirus 2 were included. Clinical data were recorded anonymously on a standardized case report form. Cases were classified as proven or probable according to the European Organization for Research and Treatment of Cancer and the Mycoses Study Group Education and Research Consortium (EORTC/MSGERC) criteria [5], with the addition of diabetes mellitus (DM) and dexamethasone prescribed for COVID-19 as host factor and positive *Mucorales* PCR in serum, blood, or plasma as mycological evidence. Date of mucormycosis diagnosis was defined by the first positive sample for mucormycosis.

Patient Consent Statement

This report is part of the NRCMA official duties approved by the Institut Pasteur Internal Review Board (2009-34/IRB) in accordance with French Law. This investigation was considered to be a public health response and the necessity of written informed consent was waived. One case has already been published [6].

RESULTS

From March 2020 to June 10, 2021, 17 patients from 11 centers developed CAM (Table 1). Sixteen (94%) patients were male and the median age was 64 (range 25–79). The median body mass index was 28 (range 19–37). During the same period, 473 353 patients have been hospitalized for COVID-19 in France [7].

Underlying Risk Factors Before Coronavirus Disease 2019

Among the 17 patients, 7 (41%) had classic EORTC/MSGERC host factors for invasive mold infections before COVID-19,

Received 3 September 2021; editorial decision 29 October 2021; accepted 4 November 2021; published online 6 November 2021.

Correspondence: Fanny Lanternier, MD, PhD, Institut Pasteur, National Reference Center for Invasive Mycoses and Antifungal, 25-28 rue du Docteur Roux - 75724 Paris Cedex 15, Paris, France (fanny.lanternier@pasteur.fr).

Open Forum Infectious Diseases®2022

© The Author(s) 2021. Published by Oxford University Press on behalf of Infectious Diseases Society of America. This is an Open Access article distributed under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs licence (https://creativecommons.org/licenses/by-nc-nd/4.0/), which permits non-commercial reproduction and distribution of the work, in any medium, provided the original work is not altered or transformed in any way, and that the work is properly cited. For commercial re-use, please contact journals.permissions@oup.com

https://doi.org/10.1093/ofid/ofab566

Downloaded from https://academic.oup.com/ofid/article/9/2/ofab566/6422599 by Institut Pasteur - CeRIS user on 09 February 2023

Table 1. Characteristics and Outcome of the Patients With COVID-19-Associated Mucormycosis

Patient	Sex	Age	Underlying Disease	EORTC/MSGERC Criteria	COVID-19 Therapy	ICU	CAM Location	Diagnosis	Species	Other Fungal Infection	CAM First-Line Therapy	Outcome Month 3
1	F	68	Dexa-DM, lung carcinoma	No	Corticosteroids	Yes, HFNC, IMV	Pulmonary	Probable	*Rhizomucor pusillus*	No	L-AmB	Death
2	M	65	HM, dexa-DM	Yes	Corticosteroids	Yes, IMV	Pulmonary	Probable	*Rhizomucor miehei*	No	No	Death
3	M	25	HM, allo-HSCT, neutropenia	Yes	Corticosteroids	Yes, HFNC, IMV	Pulmonary	Probable	*Rhizomucor* spp	No	No	Death
4	M	41	SOT, agammaglobulinemia	Yes	Corticosteroids, tocilizumab	No	ROC	Proven	*Rhizopus oryzae*	No	IVZ	Death
5	M	55	HM, auto-HSCT, neutropenia	Yes	No	Yes, HFNC, IMV	Pulmonary	Probable	*Rhizopus microsporus*	CAPA	L-AmB	Death
6	M	64	No	No	No	Yes, IMV	Digestive	Proven	*R microsporus*	No	IVZ	Alive
7	M	74	No	No	Corticosteroids	Yes, HFNC, IMV	Pulmonary	Probable	*Rhizopus delemar*	CAPA	L-AmB	Death
8	M	56	Pre-existing DM	No	Corticosteroids, tocilizumab	Yes, HFNC, IMV	ROC	Proven	*R delemar*	CAPA	L-AmB	Death
9	M	53	HM, neutropenia	Yes	No	Yes, HFNC, IMV	Disseminated	Probable	*Rhizomucor* spp	No	L-AmB	Death
10	M	66	Pre-existing DM	No	Corticosteroids	Yes	Pulmonary	Probable	NA	No	L-AmB	Alive
11	M	79	Dialysis	No	Corticosteroids	Yes, HFNC, IMV	Pulmonary	Probable	*R microsporus*	No	L-AmB	Death
12	M	65	COPD, dexa-DM	No	Corticosteroids	Yes, HFNC	Pulmonary	Probable	NA	No	No	Death
13	M	60	HM, pre-existing DM	Yes	Corticosteroids	Yes, HFNC, IMV	Disseminated	Probable	NA	CAPA	L-AmB	Death
14	M	60	No	No	No	Yes, HFNC, IMV	Digestive	Proven	*Lichteimia* spp	IC	L-AmB	Death
15	M	66	No	No	Corticosteroids	Yes, HFNC, IMV	Digestive	Proven	*R microsporus*	CAPA	No	Death
16	M	57	HM, neutropenia, dexa-DM	Yes	Corticosteroids	Yes, HNFC	Disseminated	Probable	*R microsporus*	No	No	Death
17	M	67	Underlying DM	No	Corticosteroids	Yes, IMV	Pulmonary	Probable	*R microsporus*	No	L-AmB	Death

Abbreviations: allo-HSCT, allogeneic hematological stem cell transplantation; auto-HSCT, autologous hematological stem cell transplantation; CAM, coronavirus disease 2019-associated mucormycosis; CAPA, coronavirus disease 2019-associated aspergillosis; COPD, chronic obstructive pulmonary disease; COVID-19, coronavirus disease 2019; DM, diabetes mellitus; dexa-DM, diabetes mellitus induced by dexamethasone; EORTC/MSGERC, European Organization for Research and Treatment of Cancer and the Mycoses Study Group Education and Research Consortium; F, female; HM, hematological malignancy; HSCT, hematological stem cell transplantation; HNFC, high-flow nasal cannula; IC, invasive candidiasis; ICU, intensive care unit; IMV, invasive mechanical ventilation; IVZ, isavuconazole; L-AmB, liposomal-amphotericin B; M, male; NA, not applicable; ROC, rhino-orbito-cerebral; SOT, solid organ transplant.

Downloaded from https://academic.oup.com/ofid/article/9/2/ofab566/6422599 by Institut Pasteur - CeRIS user on 09 February 2023

including 1 with solid organ transplantation and 6 (35%) with hematological malignancies (HM) [5]. Overall, 4 (24%) patients had pre-existing DM. Three (18%) patients received immunosuppressive drugs, 2 (12%) received long-term corticosteroids, and 2 (12%) were currently having antineoplastic chemotherapy. Seven (41%) patients had no classic risk factors for mucormycosis before COVID-19.

Coronavirus Disease 2019

Sixteen (94%) patients had severe COVID-19 requiring intensive care unit (ICU) care. Median time between first COVID-19 symptoms and ICU transfer was 7 days (range 0–86). Management of COVID-19 required corticosteroids for 13 (76%) patients, mainly dexamethasone, and tocilizumab for 2 (12%). Twelve (71%) patients had high-flow nasal cannula oxygen therapy, and 13 (76%) had invasive mechanical ventilation.

Four (24%) patients developed DM induced by dexamethasone for COVID-19, meaning that overall 8 patients (47%) had DM. Four (24%) patients had diabetic ketoacidosis. Eleven (65%) patients had renal failure, 8 (47%) requiring dialysis.

Mucormycosis

Coronavirus disease 2019-associated mucormycosis was diagnosed a median of 24 days (range 8–90) after COVID-19 first symptoms, 12.5 days (range 1–49) after ICU hospitalization, and 16 days (range 1–49) after corticosteroid prescription. Coronavirus disease 2019-associated mucormycosis location was mainly pulmonary (n = 9; 53%), but it was also digestive (n = 3; 18%), rhino-orbito-cerebral (n = 2; 12%), or disseminated (n = 3; 18%). Twelve patients with a pulmonary location had a chest computed tomography scan evidencing a reversed halo sign in 1 patient (8%) with HM and neutropenia, consolidation in 10 (83%) patients, including 4 (33%) with a cavitation, and 1 with nodules.

Mycology

Coronavirus disease 2019-associated mucormycosis was classified as proven in 5 (29%) patients and probable in 12 (71%). The culture grew *Mucorales* in samples from 11 (65%) patients (bronchoalveolar lavage [{BAL} n = 5] and tracheal aspirate and biopsy [n = 3, each]). *Mucorales* PCR assay (adapted from [8] in 7 centers, from [9] in 1 center, and from MycoGENIE [Ademtech, France] in 1 center) was found positive in 15 (88%) patients (serum [n = 14], BAL [n = 7], tissues [n = 3], peritoneal fluid [n = 1]). Ten patients had more than 1 positive sample (on different site). Polymerase chain reaction was the only means of diagnosis for 4 patients including 2 with positive serum and BAL samples. Histology identified hyphae compatible with *Mucorales* in biopsies from 5 patients.

Mucorales was identified to the genera or species level by culture or species-specific PCR in 14 (82%) patients, mainly (n = 9, 64%) with *Rhizopus* (*Rhizopus microsporus* [n = 6; 43%], *Rhizopus delamar* [n = 2; 14%], and *Rhizopus arrhizus* [n = 1; 7%]), secondary (n = 4, 29%) with *Rhizomucor* (*Rhizomucor pusillus*, *Rhizomucor miehei* [1 each, 7%]), and with *Lichtheimia* spp in only 1 case (7%). All species identified from both culture and PCR were concordant. The cases of *Rhizomucor* occurred in 3 patients with HM and in 1 patient with pulmonary carcinoma.

Other Fungal Infections

Five (29%) patients developed COVID-19-associated aspergillosis (CAPA), a median of 2 days (−28 to 0) before CAM. All patients with CAPA and CAM died before week 12 of mucormycosis.

Treatment and Outcome

Five (29%) patients died before the diagnosis was made and did not receive any specific treatment. Twelve (71%) patients were prescribed liposomal amphotericin B (n = 10, 59%) or isavuconazole (n = 2, 12%). Three (18%) patients had surgery; 2 for rhino-orbito-cerebral mucormycosis and 1 for colonic perforation.

Global mortality was 76% (13 of 17) at week 6 and 88% (15 of 17) at week 12. Death occurred after a median of 34 days (15–124) after the first symptoms of COVID-19 and after a median of 7 days (0–86) after the first positive sample for CAM. All 7 patients with EORTC/MSGERC criteria died within 3 weeks after the diagnosis of CAM. Twelve-week survival curves in the whole population and according to the host factors are presented in a Supplementary Figure.

DISCUSSION

In this study, we reported 17 cases of CAM in France, the largest series from 1 country outside India [4, 10]. We observed a large spectrum of clinical presentations and host factors, and we showed evidence of high mortality (88%) by 12 weeks. These findings differ from our historical (2005–2007) series of 101 mucormycoses in France (RetroZygo) and from CAM reported in India [4, 10, 11].

We compared this study with series of CAM and mucormycosis without COVID-19 from India and from the French RetroZygo study (Table 2). The frequency of underlying DM was lower in this cohort than that recorded in CAM in India (60%–95%) [4, 9]. By contrast, the frequency of hematological malignancy in CAM was higher compared with India (35% vs 1%) [10]. Clinical spectrum was different, with more frequent pulmonary (53% vs 28%) and less frequent rhino-orbito-cerebral locations (12% vs 25%) in the current series versus the historical RetroZygo Study. The presentation clearly differed from India, where CAM mainly presents with rhino-orbito-cerebral locations (>80%) [10]. This difference could be explained by higher prevalence of DM in Indian patients.

Culture and/or histology were positive in 76% of patients, whereas diagnosis of CAM was based only on a positive *Mucorales* PCR in 4 patients (24%). The broad use of *Mucorales*

Downloaded from https://academic.oup.com/ofid/article/9/2/ofab566/6422599 by Institut Pasteur - CeRIS user on 09 February 2023

Table 2. Comparison of Studies of Mucormycosis With COVID-19 (CAM) and Without COVID-19 (non-CAM) From France and India

Patient Characteristics	CAM France Present Study n (%)	CAM India Patel [10] n (%)	Non-CAM India Patel [10] n (%)	Non-CAM France Lanternier [11] n (%)
Number of patients	17	187	100	101
Age, years, mean (SD)	60 (12.5)	57 (12.5)	47 (16.4)	51 (19.9)
Sex, male, n	16 (94)	150 (80)	64 (64)	59 (58)
Underlying Diseases				
Hematological malignancy, n	6 (35)	2 (1)	2 (2)	50 (50)
Neutropenia, n	4 (24)	NA	NA	41 (41)
HSCT, n	2 (12)	NA	NA	12 (12)
Solid tumor, n	1 (6)	NA	NA	2 (2)
Solid organ transplantation, n	1 (6)	3 (2)	0	3 (3)
Diabetes mellitus, n	8 (47)	113 (60)	67 (67)	32 (32)
Trauma	0 (0)	3 (2)	9 (9)	18 (18)
Corticosteroids, n	13 (76)	146 (78)	6 (6)	NA
ICU admission, n	16 (94)	58 (31)	9 (9)	NA
CAM Location				
Pulmonary, n	9 (53)	16 (9)	6 (6)	28 (28)
ROC, n	2 (12)	161 (86)	74 (74)	25 (25)
Other, n	3 (18)	6 (3)	10 (10)	30 (30)
Disseminated, n	3 (18)	4 (2)	0	18 (18)
Diagnosis				
Culture growing *Mucorales*	11 (65)	100 (53)	38 (38)	68 (67)
Positive PCR	15 (88)	0	0	0
Histology of mucormycosis	5 (29)	143 (76)	37 (37)	NA
First-Line Therapy[a]				
Liposomal amphotericin B, n	10 (59)	136 (73)	84 (84)	68 (67)
Amphotericin B deoxycholate, n	0	31 (17)	5 (5)	6 (6)
Isavuconazole, n	2 (12)	19 (10)	2 (2)	0
Posaconazole	0	73 (39)	14 (14)	33 (33)
Surgery, n	3 (18)	131 (70)	73 (73)	(59)
Death week 12	15 (88)	75/170 (44)	42/86 (49)	43 (43)

Abbreviations: CAM, coronavirus disease 2019-associated mucormycosis; COVID-19, coronavirus disease 2019; HSCT, hematological stem cell transplantation; ICU, intensive care unit; NA, not applicable; PCR, polymerase chain reaction; ROC, rhino-orbito-cerebral; SD, standard deviation.

[a]First-line therapy includes combined antifungal therapy.

PCR could partly explain the higher frequency of CAM in France compared with other European countries [3, 8] and of some locations, mainly pulmonary or digestive, compared with the previous French Retrozygo studies, in which PCR was not used [11]. *Rhizopus microsporus* was the most frequent species in this small series. It is likely that although *Mucorales* is present in the environment, the species recovered are influenced by the geographic area, as well as the anatomic site, and the underlying risk factors, explaining the differences in species distribution among studies independently of COVID [4].

Twelve-week mortality was very high (88%) in our current CAM study, compared with the RetroZygo Study (44%), and with CAM in India (40%–50%) [4, 10, 11]. It is also higher than that reported for CAPA [1, 12]. This major difference might be partly explained by the higher frequency of pulmonary or disseminated presentations, which are classically associated with a poorer prognosis compared with rhino-orbito-cerebral locations. The severity of COVID-19 itself and the high proportion of patients hospitalized in the ICU might also account for these differences.

The differences in frequencies, comorbidities, anatomical location, and prognosis between our current series and CAM in India might be explained in part by a higher frequency of patients with DM in India [13]. Historically, there is a higher burden of mucormycosis in India. In addition to DM, we hypothesized that environmental and possibly genetic conditions might play a role in the occurrence of mucormycosis in this country independently of COVID-19. The addition of the COVID-19 pandemic, the broad use of dexamethasone, and the high frequency of DM lead to the so-called "black fungus threat" in India, which does not seem to be the case in France and other countries outside India.

Despite the multicenter design, the limitations of our study are the small number of cases and the retrospective design.

Downloaded from https://academic.oup.com/ofid/article/9/2/ofab566/6422599 by Institut Pasteur - CeRIS user on 09 February 2023

However, epidemiological surveillance in France is based on a reliable and sustained collaboration between French mycologists and the NRCMA, which limits the risk of reporting bias.

CONCLUSIONS

Coronavirus disease 2019-associated mucormycosis has a high mortality in this study. Better knowledge, identification, and earlier treatments of CAM might help to improve the prognosis. International studies are warranted to better understand and assess CAM.

Supplementary Data

Supplementary materials are available at *Open Forum Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Acknowledgments

Potential conflicts of interest. F. D. declares personal fees from Gilead outside the submitted work. F. L. declares personal fees from Gilead and F2G outside the submitted work. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

COVID-Mucor St Group

Hamid Merdji (Médecine Intensive et Réanimation, Hôpitaux Universitaires de Strasbourg, Strasbourg, France); Xavier Delabranche (Réanimation Chirugicale, Hôpitaux Universitaires de Strasbourg, Strasbourg, France); Antoine Parrot (Service de Pneumologie, Hôpital Tenon, AP-HP, Paris, France); Guillaume Voiriot (Service de Médecine Intensive et Réanimation, Hôpital Tenon, AP-HP, Paris, France), Tomas Urbina (Service de Réanimation Médicale, Hôpital Saint Antoine, AP-HP, Paris, France); Alexandre Mebazaa (Réanimation Chirurgicale, Hôpital Saint-Louis, AP-HP, Paris, France); Benjamin Chousterman (Réanimation, Hôpital Lariboisière, AP-HP, Paris, France); Ahmed El Kalioubie (Réanimation, CHU de Lille), Sophie Six (Réanimation, CHU de Lille, Lille, France); Pauline Coulon and Boualem Sendid (Service de Mycologie, CHU de Lille, France); Nadia Anguel (Réanimation Médicale, Le Kremlin-Bicêtre, AP-HP, Paris, France); Charles Damoisel (Réanimation Polyvalente, Clamart, AP-HP, France); Charlotte Mussini (Service d'Anatomopathologie, Le Kremlin-Bicêtre, AP-HP, Paris, France); Alban Villate (Hématologie, Tours, France); Jean-Christophe Navellou (Réanimation, CHU Besançon, France); Christophe Girault (Médecine Intensive et Réanimation, CHU Rouen, France); Carole Cassagne (Laboratoire de Mycologie, CHU Timone, Marseille, France); Olivier Augereau (Laboratoire de Microbiologie, Colmar, France); Francoise Dromer, Dea Garcia-Hermoso, Olivier Lortholary, Alexandre Alanio (CNRMA, Institut Pasteur, Paris, France).

References

1. Koehler P, Bassetti M, Chakrabarti A, et al. Defining and managing COVID-19-associated pulmonary aspergillosis: the 2020 ECMM/ISHAM consensus criteria for research and clinical guidance. Lancet Infect Dis **2021**; 21:e149–62.
2. Rudramurthy SM, Hoenigl M, Meis JF, et al.; ECMM and ISHAM. ECMM/ISHAM recommendations for clinical management of COVID-19 associated mucormycosis in low- and middle-income countries. Mycoses **2021**; 64:1028–37.
3. Buil JB, van Zanten ARH, Bentvelsen RG, et al. Case series of four secondary mucormycosis infections in COVID-19 patients, the Netherlands, December 2020 to May 2021. Eurosurveillance **2021**; 26:2100510.
4. Hoenigl M, Seidel D, Carvalho A, et al. The Emergence of COVID-19 Associated Mucormycosis: Analysis of Cases From 18 Countries. Rochester, NY: Social Science Research Network. Available at: https://papers.ssrn.com/abstract=3844587. Accessed 22 June 2021.
5. Donnelly JP, Chen SC, Kauffman CA, et al. Revision and update of the consensus definitions of invasive fungal disease from the European organization for research and treatment of cancer and the mycoses study group education and research consortium. Clin Infect Dis **2020**; 71:1367–76.
6. Bellanger AP, Navellou JC, Lepiller Q, et al. Mixed mold infection with *Aspergillus fumigatus* and *Rhizopus microsporus* in a severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) patient. Infect Dis Now **2021**; S2666-9919(21)00030–0.
7. Santé Publique France. COVID-19: point épidémiologique du 10 juin 2021. Available at: https://www.santepubliquefrance.fr/maladies-et-traumatismes/maladies-et-infections-respiratoires/infection-a-coronavirus/documents/bulletin-national/covid-19-point-epidemiologique-du-10-juin-2021. Accessed 12 October 2021.
8. Millon L, Herbrecht R, Grenouillet F, et al. Early diagnosis and monitoring of mucormycosis by detection of circulating DNA in serum: retrospective analysis of 44 cases collected through the French Surveillance Network of Invasive Fungal Infections (RESSIF). Clin Microbiol Infect **2016**; 22:810.e1–8.
9. Bialek R, Konrad F, Kern J, et al. PCR based identification and discrimination of agents of mucormycosis and aspergillosis in paraffin wax embedded tissue. J Clin Pathol **2005**; 58:1180–4.
10. Patel A, Agarwal R, Rudramurthy SM, et al; MucoCovi Network3. Multicenter epidemiologic study of coronavirus disease-associated mucormycosis, India. Emerg Infect Dis **2021**; 27:2349–59.
11. Lanternier F, Dannaoui E, Morizot G, et al. A Global analysis of mucormycosis in France: the retrozygo study (2005-2007). Clin Infect Dis **2012**; 54:S35–S43.
12. Gangneux JP, Dannaoui E, Fekkar A, et al. Fungal infections in mechanically ventilated patients with COVID-19 during the first wave: the French multicentre MYCOVID study. Lancet Respir Med **2021**
13. John TM, Jacob CN, Kontoyiannis DP. When uncontrolled diabetes mellitus and severe COVID-19 converge: the perfect storm for mucormycosis. J Fungi (Basel) **2021**; 7:298.

Downloaded from https://academic.oup.com/ofid/article/9/2/ofab566/6422599 by Institut Pasteur - CeRIS user on 09 February 2023