Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.
In conclusion, we report that Temozolomide can be associated with severe invasive aspergillosis, which is in all likelihood associated with T lymphocyte immune dysfunction. Physicians should be aware in regard to opportunistic infections when managing patients with glioblastoma, and patients exposed to this agent should be carefully monitored.

Human and animal rights

The authors declare that the work described has not involved experimentation on humans or animals.

Informed consent and patient details

The authors declare that they obtained a written informed consent from the patients and/or volunteers included in the article and that this report does not contain any personal information that could lead to their identification.

Disclosure of interest

The authors declare that they have competing interest.

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Author contributions

All authors attest that they meet the current International Committee of Medical Journal Editors (ICMJE) criteria for Authorship. CB and RN wrote the manuscript and performed the literature search. CB, YZ and JM were involved in patient care. CB, YZ, TC, JM and RN were involved in management of his fungal disease. TC performed the mycological antigen assay. All authors read and accepted the final version of the manuscript.

References

[1] Schwarzberg AB, Stover EH, Sengupta T, Michelini A, Vincitore M, Baden LR, et al. Selective lymphopenia and opportunistic infections in neuroendocrine tumor patients receiving temozolomide. Cancer Invest 2007;25:249–55. http://dx.doi.org/10.1080/073579007012206280.
[2] Donnelly JP, Chen SC, Kauffman CA, Steinbach WJ, Baddley JW, Verweij PE, 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 Off Publ Infect Dis Soc Am 2019. http://dx.doi.org/10.1093/cid/ciz1008.
[3] Dib RW, Khalil M, Fares J, Hachem RY, Jiayang, Dandachi D, et al. Invasive pulmonary aspergillosis: comparative analysis in cancer patients with underlying haematologic malignancies versus solid tumours. J Hosp Infect 2020;104:358–64. http://dx.doi.org/10.1016/j.jhin.2019.09.020.
[4] Damek DM, Lilleye KG, Kleinschmidt-DeMasters BK. Aspergillus terreus brain abscess mimicking tumor progression in a patient with treated glioblastoma multiforme. Clin Neuropathol 2008;27:400–7. http://dx.doi.org/10.1034/j.1468-2957.2008.00741.x.
[5] Ikeda T, Suzuki J, Norizuki M, Okabe T, Onishi T, Sasahara T, et al. Cutaneous invasive aspergillosis in a patient with glioblastoma receiving long-term temozolomide and corticosteroid therapy. J Infect Chemother Off J Jpn Soc Chemther 2017;23:253–5. http://dx.doi.org/10.1016/j.jiac.2016.10.004.
[6] Liu SA, Sullivan T, Bryce C, Chan AM, Cilmi S. Cerebral aspergillosis within new tumour site presents as incidental new brain lesion in patient receiving temozolomide for glioblastoma multiforme. BMJ Case Rep 2019;12. http://dx.doi.org/10.1136/bcr-2018-227500.
[7] Munhoz RR, Pereira Picarelli AA, Toques Mitteldorf CA, Feher O. Aspergillosis in a patient receiving temozolomide for the treatment of glioblastoma. Case Rep Oncol 2013;6:410–5. http://dx.doi.org/10.1159/000354429.
[8] Su YB, Sohn S, Krown SE, Livingston PO, Wolochok JD, Quinn C, et al. Selective CD4+ lymphopenia in melanoma patients treated with temozolomide: a toxicity with therapeutic implications. J Clin Oncol Off J Am Soc Clin Oncol 2004;22:610–6. http://dx.doi.org/10.1200/JCO.2004.07.060.
[9] Zhou W, Li H, Zhang Y, Huang M, He Q, Li P, et al. Diagnostic Value of Galactomannan Antigen Test in Serum and Bronchoalveolar Lavage Fluid Samples from Patients with Nonneutropenic Invasive Pulmonary Aspergillosis. J Clin Microbiol 2017;55:2153–61. http://dx.doi.org/10.1128/JCM.00345-17.
[10] Pazos C, Pontón J. Del Palacio A. Contribution of (1→3)-beta-D-glucan chromogenic assay to diagnosis and therapeutic monitoring of invasive aspergillosis in neutropenic adult patients: a comparison with serial screening for circulating galactomannan. J Clin Microbiol 2005;43:299–305. http://dx.doi.org/10.1128/JCM.43.1.299-305.2005.

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Novel pathogens, same old habits. A call for evidence-based research in the fight against COVID-19

Mia Wallace:
Don’t you hate that?
Vincent Vega: Hate what?
Mia Wallace: Uncomfortable silences.
Why do we feel it’s necessary to yak about bullshit in order to be comfortable?

PULP FICTION, MIRAMAX Films 1994

With the rapid spread of the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [1], journals are receiving an increasing number of papers on the issue [2].

Many of them are focused on how to improve patient management and therapeutic interventions, and a massive collective effort is being brought to bear by the scientific community to enhance currently available COVID-19 treatments, and ultimately to defeat SARS-CoV-2.

At present, before vaccines become widely available, current disease management relies on infection prevention through social distancing and increased hygiene, and supportive care involving oxygen supplementation.

The race by the scientific community to find solutions has led to a spate in scientific publication, including many papers of poor quality.

Given the paucity of reliable data about this novel virus, the organization of studies with a high level of evidence can be signally challenging.

However, even and especially in this prolonged emergency situation, it should be borne in mind that the ongoing search for effective new drugs, suitable treatment protocols and preventive strategies requires appropriate and valid trials (i.e., prospective, randomised-controlled clinical studies, international multicenter studies)
Mixed mold infection with Aspergillus fumigatus and Rhizopus microsporus in a severe acute respiratory syndrome Coronavirus 2 (SARS-CoV-2) patient

Infection mixte à Aspergillus fumigatus et Rhizopus microsporus chez un patient faisant une forme grave de COVID-19

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Mucormycose
Infection mixte

1. Introduction

In the recent context of the Coronavirus disease 2019 (COVID-19) pandemic, secondary fungal infections, such as invasive pulmonary aspergillosis, have been reported for about 30% of the cases admitted to the ICU, mostly in patients in whom the European organisation for the research and treatment of cancer: Mycoses study group education and research consortium (EORTC/MSGERC) host factors were absent [1–3]. At the university hospital of Besançon (northeastern France), while a similar proportion of putative invasive pulmonary aspergillosis was observed, we also had one case of mixed-mold infection displaying both Aspergillus fumigatus and Rhizopus microsporus isolated in the respiratory samples of an immunocompromised patient with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). We propose here to report and discuss this rare occurrence.

2. Case

A 55-year-old man was diagnosed in 2017 with follicular lymphoma, which recurred in 2018. After autologous hematopoietic stem cell transplantation (auto-HCT) was planned, the patient tested positive for Influenza B virus (Day –20). Prior to auto-HCT, a SARS-CoV-2 Real-time polymerase chain reaction (RT–PCR) test [4] was performed from a nasopharyngeal sample on Day –7 and was negative. Auto-HCT was performed on Day 0 (D0). Over the following days, the patient became feverish while in aplasia despite antibiotic treatment, and a new SARS-CoV-2 RT–PCR test from a nasopharyngeal swab came back positive with a very high respiratory viral load (D6; cycle threshold (CT) value = 9.9 and 9.7 for the 2 target genes). The patient was then transferred to the infectious diseases department. His aplasia period ended at D10. A strong inflammatory response was observed with D-Dimer at 3710 ng/mL, fibrinogen at 8.93 g/L and C-reactive protein (CRP) reaching 552 mg/L at D11. At D12, the respiratory status of the patient abruptly worsened and the patient was admitted to an intensive care unit (ICU) to receive mechanical ventilation. On D19 and D21, respiratory samples (tracheal aspirate and bronchoalveolar lavage fluid [BALF]) were positive in culture for both Aspergillus fumigatus and Rhizopus microsporus (Fig. 1). On D34, a 2nd BALF was positive in culture for A. fumigatus (Fig. 1). The parasitology–mycology department of the university hospital of Besançon developed fungal qPCR in-house techniques, targeting A.

In the absence of reliable data, premature affirmations from the scientific community about treatment efficacy should be forewarned, as they could lead to avoidable complications.

As an example, chloroquine and hydroxychloroquine have been put in the spotlight as potential game changers in COVID-19 prophylaxis and treatment [3,4]. Without available data from randomized controlled trials evidence sufficient to justify recommendations, off-label use of hydroxychloroquine for COVID-19 patients has been promoted [4]. Such incautious behaviour may entail improper use of drugs, causing harm due to side effects and overdose, and also resulting in drug shortages for patients requiring specific medications for chronic illnesses.

In addition to that, many publishers encourage projects that do not require extensive inquiry and evidence gathering. The growing burden of journals which fail to conduct peer review and have very poor scholarly quality is likely to contribute to the rise of low-quality papers.

Caution by public health professionals, world leaders, and scientific journal editors is called for. Everyone involved in the war against COVID-19 should be made to understand that anecdotal reports with limited in vitro data can be detrimental to ongoing research and that only evidence-based, rigorous and high-quality clinical data should be taken into consideration.

In the absence of reputable evidence, our best choice as a scientific community is to adhere to current guidelines, behave sensibly and, if our “expert opinion” may not be of help, exercise our right to uncomfortable silence.

Disclosure of interest

The authors declare that they have no competing interest.

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References

[1] Wang C, Horby PW, Hayden FG, Gao GF. A novel coronavirus outbreak of global health concern. Lancet 2020;395:470–4.
[2] Teixeira da Silva JA, Tsiganis P, Efranmanesh M. Publishing volumes in major databases related to Covid-19. Scientometrics 2020;2020;28:1–12.
[3] Principi N, Esposito S. Chloroquine or hydroxychloroquine for prophylaxis of COVID-19, Lancet Infect Dis 2020, http://dx.doi.org/10.1016/S1473-3099(20)30296-6.
[4] Pastick KA, Okafor EC, Wang F, et al. Review: Hydroxychloroquine and Chloroquine for Treatment of SARS-CoV-2 (COVID-19). Open Forum Infect Dis 2020;7:ofaa1130.

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