

Scedosporium apiospermum brain abscesses in a patient receiving ibrutinib and venetoclax

Rocio Figueroa¹  | Nicolas Martinez-Calle¹ | Katie Prescott² | Mark Bishton¹

¹ Clinical Haematology, Nottingham University Hospitals NHS Trust

² Pathology, Nottingham University Hospitals NHS Trust

Correspondence:

Rocio Figueroa, Clinical Haematology, Nottingham University Hospitals NHS Trust

Email: Rocio.FigueroaMora@nuh.nhs.uk

An 80-year-old male, with relapsed mantle cell lymphoma was treated on a trial with the combination of the bruton tyrosine kinase (BTK) inhibitor, ibrutinib, and BH3-mimetic, venetoclax, and achieved complete remission by both Computerized Tomography-Positron Emission Tomography (CT-PET) and molecular assessment. Despite a persistent mild neutropenia noted at study visits, which did not require drug interruption or Granulocyte-colony stimulating factor (GCSF) by protocol, he had a normal IgG level and had not suffered any infectious complications during 2 years of therapy. Following a fall at home, he presented to hospital with confusion. CT and Magnetic Resonance

Imaging (MRI) head demonstrated multifocal right frontal lobe brain abscesses requiring urgent neurosurgical drainage (Figure 1A). *Scedosporium apiospermum* was cultured from pus (Figure 1B). The isolate was sent to the Public Health England mycology reference laboratory where in vitro sensitivity to amphotericin B and voriconazole was demonstrated. The patient had no other attributable risk factors such as near drowning or prolonged steroid therapy. CT-PET did not demonstrate any evidence of systemic fungal infection and confirmed ongoing metabolic remission. Both ibrutinib and venetoclax therapy were discontinued and the patient was commenced on therapeutic

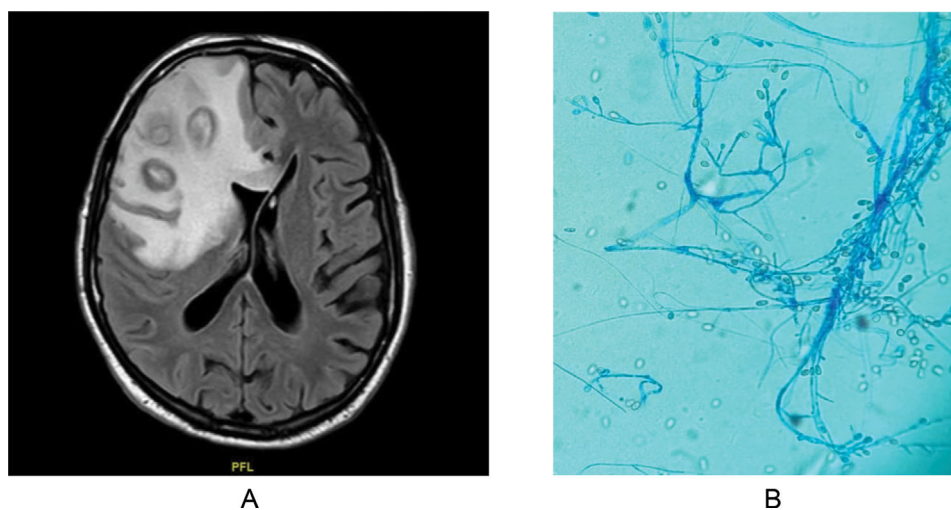


FIGURE 1 A. Long TR-FLAIR sequence Head MRI showing multiple right frontal lobe abscesses. B. Microscopic picture of *Scedosporium apiospermum* obtained from surgical drainage.

This is an open access article under the terms of the [Creative Commons Attribution](https://creativecommons.org/licenses/by/4.0/) License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited.

© 2020 The Authors. eJHaem published by British Society for Haematology and John Wiley & Sons Ltd.

voriconazole, with close therapeutic drug monitoring. Clinical and radiological improvement was observed, and the patient remains clinically well 4 months later.

Scedosporium apiospermum is a filamentous fungus found in soil and stagnant water. It can result in severe disseminated infections in immunocompromised hosts, most commonly following accidental inhalation of contaminated water. Common sites of infection include lung, bone, and the central nervous system. Treatment of these infections is challenging in view of resistance to many antifungal agents.

In addition to the inhibition of BTK in multiple immune effector cells, ibrutinib also irreversibly inhibits BTK in T cells, with resulting inhibition of T- and NK-cell function and impaired macrophage phagocytosis. Opportunistic infections such as *Aspergillus* and *Pneumocystis* have been reported with ibrutinib both as monotherapy and in combination, and herpes simplex and *Pneumocystis jirovecii* prophylaxis are considered mandatory. In contrast, opportunistic infections secondary

to venetoclax monotherapy appear rare. To our knowledge, central nervous system infection due to *S. apiospermum* has not been previously reported. Given limited published data regarding the risk of serious infection with ibrutinib/venetoclax, our case is a cautionary tale that severe infections associated with molecular targeted "chemo free" agents may occur in the absence of other risk factors and after prolonged therapy.

ORCID

Rocio Figueroa  <https://orcid.org/0000-0002-2773-4982>

How to cite this article: Figueroa R, Martinez-Calle N, Prescott K, Bishton M. *Scedosporium apiospermum* brain abscesses in a patient receiving ibrutinib and venetoclax. *eJHaem*. 2020;1:418–419. <https://doi.org/10.1002/jha2.121>