Infect Chemother. 2022 Sep;54(3):545-546
https://doi.org/10.3947/ic.2022.0046
pISSN 2093-2340·eISSN 2092-6448

Infection & Chemotherapy

Correspondence

Tigecycline for Severe Rickettsioses: Gained Experience Needing a Slight Grain of Salt

Lucas S. Blanton [1] **and Álvaro A. Faccini-Martínez** [2]

[1]Department of Internal Medicine – Infectious Diseases, University of Texas Medical Branch, Galveston, TX, USA
[2]Committee of Tropical Medicine, Zoonoses and Travel Medicine, Asociación Colombiana de Infectología, Bogotá, Colombia

▸ See the article "Does Tigecycline Have a Place in Therapy for Rickettsial Infection of the Central Nervous System?" in volume 54 on page 165.

Received: Apr 14, 2022
Accepted: Apr 21, 2022
Published online: Jul 12, 2022

Corresponding Author:
Lucas S. Blanton, MD
Department of Internal Medicine – Infectious Diseases, University of Texas Medical Branch, 301 University Boulevard, Galveston, TX 77555-0435, USA.
Tel: +409-747-0236
Fax: +409-772-6527
Email: lsblanto@utmb.edu

ORCID iDs
Lucas S. Blanton
https://orcid.org/0000-0002-4653-2323
Álvaro A. Faccini-Martínez
https://orcid.org/0000-0002-1127-0132

Funding
None.

Dear Editor:

We read with interest the article by Mastroianni and colleagues titled "Does Tigecycline Have a Place in Therapy for Rickettsial Infection of the Central Nervous System [1]." In this report, the authors describe their experience using tigecycline to treat those with neurologic manifestations of spotted fever group (SFG) rickettsiosis in Italy. In their series of 5 patients, they report a favorable response to the use of high dose tigecycline (200 mg loading dose followed by 100 mg administered twice daily). Tigecycline, a relatively unproven antibiotic for clinical rickettsioses, has *in vitro* activity against several tested rickettsiae [2, 3] and appears effective in an animal model for lethal Rocky Mountain spotted fever (RMSF) [3]. Although doxycycline is the agent of choice, manifestations such as nausea/vomiting or concern for impaired absorption associated with critical illness, may preclude its oral use. Unfortunately, as highlighted by this article, the parenteral formulation is not always available in some regions [1, 3]. Sharing clinical therapeutic experience through publication of observational studies is of importance when controlled trials are not feasible, so the case series by Mastroianni et al. [1] may be very helpful to clinicians faced with severe manifestations of SFG rickettsioses without the availability of intravenous doxycycline.

It is important to note that these cases described by Mastroianni et al. [1] do not represent RMSF though. RMSF is caused by *Rickettsia rickettsii*, an organism strictly endemic to the Americas [4]. Rather, the authors are most likely describing illness caused by *Rickettsia conorii* (Mediterranean spotted fever [MSF]). Like RMSF, manifestations of MSF can be severe with neurologic signs and symptoms [5]. Other SFG rickettsiae are also distributed in Italy (*e.g.*, *Rickettsia massiliae* and *Rickettsia monacensis*) and have been documented to cause illness, albeit generally not as severe as MSF [4, 6]. In addition to *R. rickettsii* being absent from Italy, it is generally not associated with formation of an inoculation eschar, a finding often found in those with MSF [7], as documented in 2 of the patients described in this series [1].

The 5 patients described were all laboratory confirmed via 4-fold increase in antibody titer from paired sera (reportedly separated by 2 weeks), but antibodies stimulated by a SFG rickettsial species will react against antigen derived from other SFG rickettsiae [4]. Without

Conflict of Interest
No conflict of interest.

Author Contributions
Conceptualization: LSB, ÁAFM. Writing - original draft: LSB, ÁAFM. Writing - review & editing: LSB, ÁAFM.

cumbersome cross absorption techniques performed on reactive sera or through use of molecular methods, a species-specific diagnosis is not obtainable through standard serologic methods (*i.e.*, indirect immunofluorescence assay or enzyme-linked immunosorbent assay) [8]. Thus, the regional epidemiology becomes very important when interpreting serologic results. MSF can be quite severe, but the case fatality rate in the antibiotic era is generally lower than that of RMSF (2.5% *vs.* 4.0 – 8.0%, respectively) [7]. Thus, the optimism for tigecycline's clinical effectiveness in RMSF must be tempered due to the lack of clinical data with this entity. Despite this point, the experience shared in this series [1] and others (tigecycline has been successfully used in a severe case of *Rickettsia australis* [9] and *Rickettsia typhi* infection [10]) is valuable for clinicians when intravenous doxycycline is unavailable.

REFERENCES

1. Mastroianni A, Greco S, Urso F, Mauro MV, Vangeli V. Does tigecycline have a place in therapy for rickettsial infection of the central nervous system? Infect Chemother 2022;54:165-72.
PUBMED | CROSSREF
2. Quade BR, Ramírez-Hernández A, Blanton LS. *In vitro* susceptibility of *Rickettsia* species to eravacycline, omadacycline, and tigecycline. Antimicrob Agents Chemother 2021;65:e0066521.
PUBMED | CROSSREF
3. Blanton LS, Wilson NM, Quade BR, Walker DH. Susceptibility of *Rickettsia rickettsii* to tigecycline in a cell culture assay and animal model for rocky mountain spotted fever. Am J Trop Med Hyg 2019;101:1091-5.
PUBMED | CROSSREF
4. Parola P, Paddock CD, Socolovschi C, Labruna MB, Mediannikov O, Kernif T, Abdad MY, Stenos J, Bitam I, Fournier PE, Raoult D. Update on tick-borne rickettsioses around the world: a geographic approach. Clin Microbiol Rev 2013;26:657-702.
PUBMED | CROSSREF
5. Sekeyová Z, Danchenko M, Filipčík P, Fournier PE. Rickettsial infections of the central nervous system. PLoS Negl Trop Dis 2019;13:e0007469.
PUBMED | CROSSREF
6. Gomez-Barroso D, Vescio MF, Bella A, Ciervo A, Busani L, Rizzo C, Rezza G, Pezzotti P. Mediterranean spotted fever rickettsiosis in Italy, 2001-2015: Spatio-temporal distribution based on hospitalization records. Ticks Tick Borne Dis 2019;10:43-50.
PUBMED | CROSSREF
7. Blanton LS, Walker DH. *Rickettsia rickettsii* and other spotted fever group rickettsiae (Rocky Mountain spotted fever and other spotted fevers). In: Bennett JE, Dolin R, Blaser MJ, eds. Mandell, Douglas, and Bennett's principles and practice of infectious diseases. 9th ed. Philadelphia: Elsevier; 2020;2349-57.
8. Paris DH, Dumler JS. State of the art of diagnosis of rickettsial diseases: the use of blood specimens for diagnosis of scrub typhus, spotted fever group rickettsiosis, and murine typhus. Curr Opin Infect Dis 2016;29:433-9.
PUBMED | CROSSREF
9. Wilson PA, Tierney L, Lai K, Graves S. Queensland tick typhus: three cases with unusual clinical features. Intern Med J 2013;43:823-5.
PUBMED | CROSSREF
10. Luciani F, Cione E, Corsonello A, Guido F, De Santis S, Cannataro R, Perri M, Caroleo MC, Cannataro AM. Spotted fever from Rickettsia typhi in an older woman: a case report from a geographic area where it would not be expected. Int J Infect Dis 2014;27:10-2.
PUBMED | CROSSREF