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Rickettsioses as Underrecognized Cause of Hospitalization for Febrile Illness, Uganda

Appendix

Supplementary Methods

After presentation to the emergency department or outpatient department and designation for hospitalization, patients received informed consent in IRB-approved parent protocols. Rash was assessed as part of a clinical exam consistent with standard practice (excluding a full skin exam) and prospectively recorded if present using a standardized report form. Clinical tests were routinely performed including complete blood counts and chemistries. Microbiologic testing included blood culture with antimicrobial sensitivity testing, HIV testing, malaria smears and rapid diagnostic tests; all were routinely performed as previously described (1) (P.W. Blair, et al., unpub. data, https://www.medrxiv.org/content/10.1101/2023.09.14.23295526v1). If there was clinical suspicion, PCR testing for tuberculosis was performed using expectorated sputum (Cepheid) and participants living with HIV had a urine lipoarabinomannan (LAM test). Whole blood was run on the FilmArray Global Fever (BioFire) panel for 19 non-rickettsial pathogen targets (2).

Appendix Table. Exclusivity testing with SYBR-green PCR using DNA from multiple clinically relevant species. Isolates with a PCR curve and melting curve separate from the non-template control indicated as positive.

Group	Species	Result
Spotted fever group rickettsia	R. akari	Positive
	R. conorii	Positive
	R. felis	Positive
	R. montanensis	Positive
	R. parkeri	Positive
	R. peacockii	Positive
	R. rickettsii	Positive
	R. siberica	Positive
Typhus group rickettsia	R. typhi	Positive
Ehrlichia spp.	E. chaffeensis	Negative
	E. muris eauclairensis	Negative
Anaplasma spp.	A. capra	Negative
	A. phagocytophilum	Negative
Orientia spp.	O. tsutsugamushi	Negative
Candida spp.	Pichia kudriavzevii (formerly Candida krusei)	Negative

Group	Species	Result
Enteric bacteria	E. coli	Negative
	Ps. aeruginosa	Negative
Staphylococcus spp.	S. aureus	Negative

References

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- 2. Manabe YC, Betz J, Jackson O, Asoala V, Bazan I, Blair PW, et al. Clinical evaluation of the BioFire Global Fever Panel for the identification of malaria, leptospirosis, chikungunya, and dengue from whole blood: a prospective, multicentre, cross-sectional diagnostic accuracy study. Lancet Infect Dis. 2022;22:1356–64. <u>PubMed</u>