

# *Rickettsia mongolitimonae* Encephalitis, Southern France, 2018

## Appendix

**Appendix Table.** Encephalitis and *Rickettsia* spp.\*

Case	Epidemiologic data			Age/s ex	Previous illness	Clinical manifestation		CFS, CT scan, MRI	Diagnostic test	Treatment	Outcome	Ref
	Country	Rural	Date			General	Neurologic					
<i>Rickettsia conorii</i>												
1	Italy	NA	2013 Aug	78 y/F	Arterial hypertension, type 2 diabetes, stroke	Fe + R + S, renal failure	Coma GCS3	–CFS: meningitis –CT scan: normal –MRI: ND	IFA, ELISA	Chloramphenicol, levofloxacin, corticosteroids	Death	(1)
2	Portugal	Dogs	2010 Sep	59 y/M	None	Fe + R + S, myalgia	Headache, hemisensory loss	–CFS: no meningitis –CT scan: hypodensities frontal lobes and 1 lesion in left ventricle –MRI: multiple noncontrast enhancement, periventricular	IFA	Doxycycline 200 mg/12 h 4 d, doxycycline 100 mg/12 h 3 d	Hemisensory loss on the left	(2)
3	Morocco	Dogs	2009	1.2 y/M	None	Fe + R + S	Convulsions	–CFS: meningitis –CT scan: normal –MRI: normal	IFA	Josamycin 12 h, corticosteroids	Bilateral decreased vision, seizures	(3)
4	Spain	Dogs	2008 Jun	66 y/M	Type 2 diabetes	Fe + R + S, myalgia, renal failure, thrombocytopenia	Headache, confusion, quadriplegia, aphasia	–CFS: no meningitis –CT scan: normal –MRI: diffuse lesions in frontal, parietal, occipital, corpus callosum, cerebellar peduncles, pons, and limbic area	IFA	Doxycycline 100 mg/12 h 10 d	Aphasia and right hemiplegia	(4)
5	Morocco	NA	2004 Jul	49 y/F	None	Fe + R	Headache, confusion	–CFS: meningitis –CT scan: normal –MRI: meningeal contrast enhancement and lesion in right frontal lobe	IFA	Ceftriaxone, ampicillin, doxycycline	Remission	(5)

Case	Epidemiologic data			Age/s ex	Previous illness	Clinical manifestation		CFS, CT scan, MRI	Diagnostic test	Treatment	Outcome	Ref
	Country	Rural	Date			General	Neurologic					
6	India	Dogs	2009	4 y/F	None	Fe + R	Convulsions	–CFS: meningitis –CT scan: normal –MRI: ND	Weil-Felix, IFA	Chloramphenicol 75 mg/kg/d in 4 doses and doxycycline 2.2 mg/kg/12 h 10 d	Remission	(6)
7	Portugal	NA	2003 Summer	47 y/M	None	Fe + R + S, myalgia, renal failure, thrombo- cytopenia	Headache, convulsions, shock	–CFS: ND –CT scan: normal –MRI: ND	Immuno- histochemistry	None	Death	(7)
8	Spain	NA	2002	27 y/F	None	Fe, myalgia, nausea, abdominal pain	Headache, paresis on left side, convulsions	–CFS: no meningitis –CT scan: normal –MRI: contrast enhancement in the meninges and right parasyllian lesion	IFA	Valproate, clonazepam, ceftriaxon, acyclovir, doxycycline, phenobarbital, corticotherapy	Remission	(8)
9	Spain	None	1999 Jul	53 y/F	Adult celiac disease	Fe + R, myalgia, arthralgia, thrombo- cytopenia, hypotension	Confusion, paraplegia	–CFS: meningitis –CT scan: normal –MRI: lesions in left frontal lobe, cerebellar peduncles, and corpus callosum	IFA	Cefotaxime, acyclovir, isoniazid, rifampin, ethambutol, streptomycin, doxycycline, methylprednisolon e	Paraplegia	(9)
10	Spain	NA	1994 Summer	65 y/M	Type II diabetes	Fe + R + S, myalgia	Confusion, incontinence, ataxia	–CFS: meningitis. –CT scan: hypodensity in white matter –MRI: ND	IFA	Doxycycline 100 mg/12 h 7 d	Remission	(10)
11	Morocco	NA	1991 Jul	6 y/M	None	Fe + R + S, arthralgia	Confusion, convulsions	–CFS: meningitis. –CT scan: hypodensity in both internal capsules –MRI: ND	IFA	Thiamphenicol 15 d, corticosteroids 21 d	Mutism and quadriplegia	(11)
12	Spain	NA	1987 Summer	77 y/F	Arterial hypertension, type 2 diabetes	Fe + R + S, myalgia, renal failure, thrombo- cytopenia.	Headache, stupor, shock	–CFS: ND –CT scan: ND –MRI: ND	IFA	Amoxicillin 11 d, tetracycline 1 d	Death	(12)
13	France	Dogs	1984 Aug	20 d/F	None	Fe + R + S, hepatomegaly, splenomegaly, thrombo- cytopenia	Inactivity, convulsion	–CFS: meningitis –CT scan: ND –MRI: ND	IFA	Ampicillin, gentamicin, spiramycin	Death	(13)

Case	Epidemiologic data			Age/s ex	Previous illness	Clinical manifestation		CFS, CT scan, MRI	Diagnostic test	Treatment	Outcome	Ref
	Country	Rural	Date			General	Neurologic					
<i>Rickettsia japonica</i>												
14	Japan	Brushy vegetation	1992 Aug	58 y/M	NA	Fe + R + S, nausea vomiting	Confusion	–CFS: meningitis –CT scan: Normal –MRI: NA	IFA	Cefmetazole, clindamycin, aztreonam, imipenem, minocycline	Remission	(14)
15	Japan	Bamboo tree	1998 Apr	55 y/M	NA	Fe + R, myalgia, nausea, vomiting, renal failure, shock	Headache, confusion, convulsions	– CFS: meningitis –CT scan: subdural hematoma –MRI: NA	IFA	Panipenem, acyclovir, minocycline	Death	(15)
16	Japan	NA	Aug	77 y/M	NA	Fe + R + S	Confusion, convulsions	NA	IFA	Minocycline	Remission	(15)
17	Japan	NA	Aug	78 y/M	NA	Fe + R, thrombo- cytopenia	NA	NA	IFA	Minocycline	Remission	(15)
<i>Rickettsia slovaca</i>												
18	Slovakia	Garden	1978 May	33 y/F	None	Fe, myalgia, arthralgia, nausea, hepatomegaly	Headache, paresthesia, bradypsychia	–CFS: no meningitis –CT scan: ND –MRI: NA	IFA	Tetracycline, doxycycline	Minimum hemiparesia	(16)
<i>Rickettsia rickettsii</i>												
19	USA	Dog, horses, chickens, parrots, rats, mice	1993 Aug	45 y/F	None	Fe + R + S, myalgia, thrombo- cytopenia	Confusion, convulsions, disorientation	–CFS: no meningitis –CT scan: white matter hypodensity and diffuse cerebral edema –MRI: multiple punctata area of increased signal through cerebral white matter	IFA	Imipenem, doxycycline	Remission	(17)
20	USA	NA	1997	68 y/M	None	Fe + R, thrombo- cytopenia	Confusion, disorientation	–CFS: no meningitis –CT scan: normal –MRI: symmetrical zones of hyperintensity in periventricular white matter	IFA	Doxycycline	Attentional deficits, visuospatial difficulties and global impairment in memory	(18)
21	USA	Farm	1999	7 y/M	None	Fe + R + S, myalgia, arthralgia	Headache, lethargy, convulsions	–CFS: meningitis –CT scan: NA –MRI: multiple foci of hyperintensity in white matter	IFA	Doxycycline, methylprednisolone	Deficit in short-term memory	(19)
22	USA	NA	2016 Apr	15 y/F	None	Fe + R	Convulsions	–CFS: NA –CT scan: NA	IFA	Doxycycline	Speech difficulty	(20)

Case	Epidemiologic data			Age/s ex	Previous illness	Clinical manifestation		CFS, CT scan, MRI	Diagnostic test	Treatment	Outcome	Ref
	Country	Rural	Date			General	Neurologic					
23	USA	Dog, cat	1997 Jun	43 y/F	None	Fe + R + S, occipital lymph node, thrombo- cytopenia, respiratory distress, acute myocardial infarction	Headache, confusion, aphasia, tetraparesia	–MRI: multiple foci of hyperintensity in periventricular white matter –CFS: meningitis –CT scan: diffuse cerebral edema with cerebellar herniation –MRI: NA	IFA	Ceftriaxone, doxycycline, methylprednisolon e	Death	(21)
24	USA	NA	2015 Jun	7 y/F	None	Fe + R + S, thrombo- cytopenia, renal failure, respiratory distress	Headache, disorientation , aphasia, dystonic posture	–CFS: no meningitis –CT scan: diffuse supratentorial attenuation –MRI: diffuse hyperintense lesion in white matter	IFA	Ceftriaxone, vancomycin, doxycycline	Aphasia	(22)

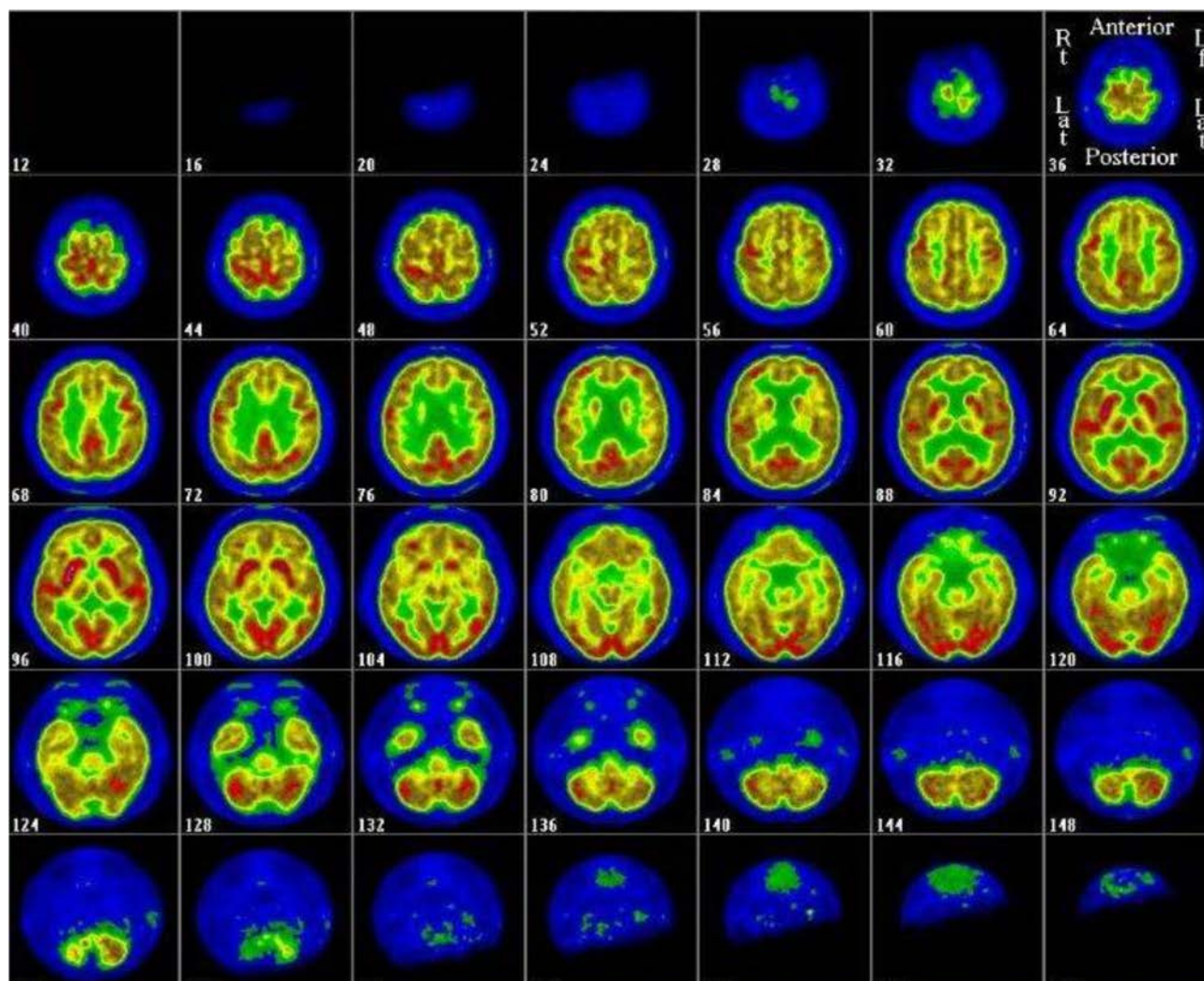
\*CSF, cerebrospinal fluid; CT, computed tomographic; Fe: fever, GCS: Glasgow coma score; CT: computed tomography ; MRI: magnetic resonance imaging ; NA: not available; IFA, immunofluorescence assay; NA, not available; ND, not done; R, rash; ref, reference; S, scar.

## References

1. Colomba C, Imburgia C, Trizzino M, Titone L. First case of Mediterranean spotted fever-associated rhabdomyolysis leading to fatal acute renal failure and encephalitis. *Int J Infect Dis.* 2014;26:12–3. [PubMed http://dx.doi.org/10.1016/j.ijid.2014.01.024](http://dx.doi.org/10.1016/j.ijid.2014.01.024)
2. Duque V, Ventura C, Seixas D, Barai A, Mendonça N, Martins J, et al. Mediterranean spotted fever and encephalitis: a case report and review of the literature. *J Infect Chemother.* 2012;18:105–8. [PubMed http://dx.doi.org/10.1007/s10156-011-0295-1](http://dx.doi.org/10.1007/s10156-011-0295-1)
3. Bougteba A, Basir A, Charradi N. Meningoencephalitis caused by *Rickettsia conorii* in a young infant [in French]. *Rev Neurol (Paris).* 2011;167:173–6. [PubMed http://dx.doi.org/10.1016/j.neurol.2010.07.010](http://dx.doi.org/10.1016/j.neurol.2010.07.010)
4. Aliaga L, Sánchez-Blázquez P, Rodríguez-Granger J, Sampedro A, Orozco M, Pastor J. Mediterranean spotted fever with encephalitis. *J Med Microbiol.* 2009;58:521–5. [PubMed http://dx.doi.org/10.1099/jmm.0.004465-0](http://dx.doi.org/10.1099/jmm.0.004465-0)
5. Demeester R, Claus M, Hildebrand M, Vlieghe E, Bottieau E. Diversity of life-threatening complications due to Mediterranean spotted fever in returning travelers. *J Travel Med.* 2010;17:100–4. [PubMed http://dx.doi.org/10.1111/j.1708-8305.2009.00391.x](http://dx.doi.org/10.1111/j.1708-8305.2009.00391.x)
6. Tikare NV, Shahapur PR, Bidari LH, Mantur BG. Rickettsial meningoencephalitis in a child—a case report. *J Trop Pediatr.* 2010;56:198–200. [PubMed http://dx.doi.org/10.1093/tropej/fmp065](http://dx.doi.org/10.1093/tropej/fmp065)
7. Amaro M, Bacellar F, França A. Report of eight cases of fatal and severe Mediterranean spotted fever in Portugal. *Ann N Y Acad Sci.* 2003;990:331–43. [PubMed http://dx.doi.org/10.1111/j.1749-6632.2003.tb07384.x](http://dx.doi.org/10.1111/j.1749-6632.2003.tb07384.x)
8. Parra-Martínez J, Sancho-Rieger J, Ortiz-Sánchez P, Peset V, Brocalero A, Castillo A, et al. Encephalitis caused by *Rickettsia conorii* without exanthema [in Spanish]. *Rev Neurol.* 2002;35:731–4. [PubMed](http://dx.doi.org/10.1016/j.neurol.2002.07.010)
9. Ezpeleta D, Muñoz-Blanco JL, Taberner C, Giménez-Roldán S. Neurological complications of Mediterranean boutonuse fever. Presentation of a case of acute encephalomyelitis and review of the literature [in Spanish]. *Neurologia.* 1999;14:38–42. [PubMed](http://dx.doi.org/10.1016/j.neurol.1999.01.010)

10. Marcos Dolado A, Sánchez Portocarrero J, Jiménez Madridejo R, Pontes Navarro JC, García Urrea D. Meningoencephalitis due to *Rickettsia conorii*. Etiopathological, clinical and diagnostic aspects [in Spanish]. *Neurologia*. 1994;9:72–5. [PubMed](#)
11. Benhammou. Fièvre Boutonneuse Méditerranéenne révélée par une atteinte neurologique grave. *Archives Francaises Pédiatriques*. 1991;48:635–6.
12. Walker GA, Masters KS, Shah DN, Anseth KS, Leinwand LA. Valvular myofibroblast activation by transforming growth factor-beta: implications for pathological extracellular matrix remodeling in heart valve disease. *Circ Res*. 2004;95:253–60. [PubMed](#)  
<http://dx.doi.org/10.1161/01.RES.0000136520.07995.aa>
13. Texier P, Rousselot JM, Quillerou D, Aufrant C, Robain D, Foucaud P. Fièvre boutonneuse méditerranéenne: à propos d'un cas mortel chez un nouveau-né. *Archives Francaises Pédiatriques*. 1984;41:51–3.
14. Araki M, Takatsuka K, Kawamura J, Kanno Y. Japanese spotted fever involving the central nervous system: two case reports and a literature review. *J Clin Microbiol*. 2002;40:3874–6. [PubMed](#) <http://dx.doi.org/10.1128/JCM.40.10.3874-3876.2002>
15. Kodama K, Senba T, Yamauchi H, Nomura T, Chikahira Y. Clinical study of Japanese spotted fever and its aggravating factors. *J Infect Chemother*. 2003;9:83–7. [PubMed](#) <http://dx.doi.org/10.1007/s10156-002-0223-5>
16. Mittermayer T, Brezina R, Urvölgyi J. First report of an infection with *Rickettsia slovaca*. *Folia Parasitol (Praha)*. 1980;27:373–6. [PubMed](#)
17. Baganz MD, Dross PE, Reinhardt JA. Rocky Mountain spotted fever encephalitis: MR findings. *AJNR Am J Neuroradiol*. 1995;16(Suppl):919–22. [PubMed](#)
18. Bergeron JW, Braddom RL, Kaelin DL. Persisting impairment following Rocky Mountain spotted fever: a case report. *Arch Phys Med Rehabil*. 1997;78:1277–80. [PubMed](#) [http://dx.doi.org/10.1016/S0003-9993\(97\)90345-2](http://dx.doi.org/10.1016/S0003-9993(97)90345-2)
19. Wei TY, Baumann RJ. Acute disseminated encephalomyelitis after Rocky Mountain spotted fever. *Pediatr Neurol*. 1999;21:503–5. [PubMed](#)  
[http://dx.doi.org/10.1016/S0887-8994\(99\)00028-4](http://dx.doi.org/10.1016/S0887-8994(99)00028-4)

20. Wittler RR, Minns GO. An adolescent with fever, rash, and altered mental status. *Clin Infect Dis*. 2016;62:1610–1. [PubMed](#)  
<http://dx.doi.org/10.1093/cid/ciw096>
21. Samuels MA, Newell KL. Case records of the Massachusetts General Hospital. Weekly clinicopathological exercises. Case 32-1997. A 43-year-old woman with rapidly changing pulmonary infiltrates and markedly increased intracranial pressure. *N Engl J Med*. 1997;337:1149–56. [PubMed](#)  
<http://dx.doi.org/10.1056/NEJM199710163371608>
22. Sun LR, Huisman TAGM, Yeshokumar AK, Johnston MV. Ongoing cerebral vasculitis during treatment of Rocky Mountain spotted fever. *Pediatr Neurol*. 2015;53:434–8. [PubMed](#) <http://dx.doi.org/10.1016/j.pediatrneurol.2015.07.003>



**Appendix Figure.** PET scan imaging showing a cerebral cortical diffuse hypometabolism.