Scalp Eschar and Neck Lymphadenopathy Caused by *Bartonella henselae* after Tick Bite

Emmanouil Angelakis,[1] Céline Pulcini,[2] Julie Waton,[3] Patrick Imbert,[4] Cristina Socolovschi,[1] Sophie Edouard,[1] Pierre Dellamonica,[2] and Didier Raoult[1]

[1]Unité de Recherche de Maladies Infectieuses Transmissibles et Emergents UMR 6236, Centre National de Références Scientifques–Institut de Recherche pour le Développement, Faculté de Médecine et de Pharmacie, Marseille, [2]Service d'Infectiologie Centre Hospitalier de l'Université (CHU) de Nice, Hôpital l'Archet, Nice, [3]Service Dermatologie, Hôpital Fournier–CHU Nancy, Nancy, and [4]Service des Maladies Infectieuses et Tropicales, Hôpital Instruction Armée Bégin, Paris, France

***Rickettsia slovaca* and *Rickettsia raoultii* have been associated with a syndrome characterized by scalp eschar and neck lymphadenopathy following tick bites. However, in many cases, the causative agent remains undetermined. We report 3 cases of this syndrome caused by *Bartonella henselae,* and we propose the term "SENLAT" to collectively describe this clinical entity.**

In 1997, *Rickettsia slovaca* was identified as the cause of a clinical entity associated with scalp eschar and neck lymphadenopathy after tick bite [1]. Lakos proposed the name "TIBOLA" (tick-borne lymphadenopathy) to describe a series of 27 patients who were likely infected with *R. slovaca,* with scalp eschar and lymphadenopathy [2]. In 2002, Raoult et al [1] reported a series of 67 patients with the same findings, of whom only 17 had definitive evidence of *R. slovaca* infection. The same year, Lakos [2] identified only 19 cases of *R. slovaca* infection among 73 patients with scalp eschar and neck adenopathy. In Spain, a similar disease, named "DEBONEL" (*Dermacentor*-borne necrosis-erythema-lymphadenopathy) was described in patients with scalp eschars and painful regional lymphadenopathy [3]. We propose the name "SENLAT" (scalp eschar and neck lymphadenopathy after tick bite) to describe this syndrome. However, these infections were not definitely confirmed to be due to *R. slovaca.*

Received 27 July 2009; accepted 19 October 2009; electronically published 13 January 2010.

Reprints or correspondence: Dr Didier Raoult (Didier.raoult@gmail.com).

Clinical Infectious Diseases 2010; 50:549–51

1058-4838/2010/5004-0015$15.00
DOI: 10.1086/650172

In 2005, Ibarra et al [3] proposed that some cases of SENLAT are probably caused by other *Rickettsia* species, and in 2006, they identified DNA of what is now known to be *Rickettsia raoultii* in blood specimens obtained from a patient. Recently, Parola et al [4] also confirmed that *R. raoultii* can cause SENLAT. They also found 2 patients who were coinfected with *R. slovaca* and *Coxiella burnetii* in an acute form of Q fever. However, in 28 patients, the specific bacterial agent causing this syndrome was not determined. These data indicate collectively that other causes of the syndrome characterized by scalp eschar and neck adenopathy remain unknown. As a national reference center for rickettsioses and bartonelloses, we receive skin biopsy and serum specimens from patients with SENLAT. These specimens are routinely tested for *Rickettsia* species, *Bartonella* species, *C. burnetii, Borrelia burgdorferi,* and *Francicella tularensis* by using serologic, molecular, and culture-based techniques.

Methods. From January 2008 through June 2009, we tested 28 patients for SENLAT, including 6 male patients and 22 female patients, who ranged from 3 years to 58 years of age. Tick bites occurred most frequently during October and November (11 [39%] of 28) and during April and May (10 [36%] of 28). No cases occurred between June and September. Western blot and cross-adsorption analyses allowed the detection of antibodies specifically directed against *R. slovaca* and *R. raoultii;* antibodies were present in 15 (53%) of 28 patients and 3 (10.7%) of 28 patients, respectively. The specific bacterial agent causing SENLAT was not determined for 7 patients (25%). However, for 3 patients (10.7%), we identified infection due to *Bartonella henselae* (Table 1).

From each of these 3 patients, we received an eschar biopsy specimen and paired serum samples. For 1 patient, we also received a tick that had been removed from the patient's scalp. Epidemiological and clinical data were also collected. DNA was extracted from the tissue biopsy specimens and from the tick using a QIAamp tissue kit (Qiagen). The DNA was used as a template in a previous described reverse-transcription (RT) polymerase chain reaction (PCR) assay targeting a portion of the *Bartonella* 16S-23S intergenic spacer region, as well as the PAP31 gene, for the detection of *B. henselae* [5]; the RKND03 gene, for the detection of *Rickettsia* species; and 12S rRNA, to identify the tick [6]. Immunoglobulin (Ig) G and IgM antibody titers reactive with spotted fever and typhus group rickettsiae, *Bartonella* species, *B. burgdorferi, F. tularensis,* and *C. burnetii* antigens were determined by an immunofluorescence antibody assay (IFA) and validated by Western blot [7]. Detailed histories for each patient are described below.

Table 1. Three Cases of SENLAT (Scalp Eschar and Neck Lymphadenopathy after Tick Bite) Caused by *Bartonella henselae*

Patient	Tick species	Tick bite	Animal exposure	Clinical manifestations	Serological test result	Western blot result	PCR result
Patient 1	*Dermacentor* species	Yes	No	Asthenia, scalp eschar, and bilateral cervical lymphadenopathy	Negative	Positive for *B. henselae*	Tick was positive for *B. henselae*
Patient 2	Unknown	Yes	Cats and horses	Asthenia, scalp eschar, and bilateral cervical lymphadenopathy	Positive for *Bartonella* species	Positive for *B. henselae*	Eschar was positive for *B. henselae*
Patient 3	Unknown	Yes	Cat, horses, and cows	Asthenia, scalp eschar, and left occipital lymphadenopathy	Positive for *Bartonella* species	Positive for *B. henselae*	Eschar was positive for *B. henselae*

NOTE. PCR, polymerase chain reaction.

Case report. Patient 1 was a 35-year-old pregnant woman with asthenia who had been bitten by a female tick on the scalp in May 2009. PCR analysis of the tick using a 12S rRNA sequence revealed that the species was *Dermacentor marginatus* (GenBank AM410570). The patient did not own a pet and did not report contact with animals. During the examination, an eschar was found at the site of the tick bite that was associated with bilateral cervical lymphadenopathy but no other specific findings. By using a real-time PCR assay, segments of the *B. henselae* intergenic spacer region and PAP31 genes were identified in the tick specimen. The eschar biopsy was performed ~1.5 months after the tick bite and was negative for *B. henselae* DNA when tested with the real-time PCR assay. *Rickettsia* DNA was not identified in the tick or the skin biopsy specimen. No antibodies reactive with *Bartonella* species, *C. burnetii, B. burgdorferi, Rickettsia* species, or *F. tularensis* were detected by IFA; however, Western blot was positive for *B. henselae*. The patient was treated with josamycine for 15 days, and after 1 month, the eschar and the lymphadenopathy had disappeared. No alopecia at the eschar site was observed.

Patient 2 was a 48-year-old female equestrian who had been bitten by a tick in November 2008 and who developed persistent asthenia. She described frequent contacts with cats and horses. Physical examination revealed an eschar on her scalp, bilateral cervical lymphadenopathy, and no other specific findings. Blood cell counts and liver enzyme levels were normal. *B. henselae* DNA was detected in the eschar biopsy specimen by PCR; no *Rickettsia* DNA was present in the specimen. A serum sample demonstrated antibodies reactive only with *B. henselae* (IgG titer, 1:512) and was negative for *C. burnetii, B. burgdorferi, Rickettsia* species, and *F. tularensis;* the result was confirmed by Western blot. The patient was treated with doxycycline, and her lymphadenopathy resolved within 2 weeks. No alopecia at the eschar site was observed.

Patient 3 was a 20-year-old man who presented with asthenia, an eschar on the scalp, and left occipital lymphadenopathy. The patient owned a cat and also had contact with horses and cows. He mentioned that he was probably bitten by a tick during November 2008. Physical examination revealed numerous tick bites, although no other specific findings were found. Blood cell counts and liver enzyme levels were normal. *B. henselae* DNA was identified by RT-PCR in the skin biopsy specimen of the eschar. RT-PCR was negative for *Rickettsia* species. A serum sample demonstrated antibodies reactive only with *B. henselae* (IgG titer, 1:2048) and negative for *C. burnetii, B. burgdorferi, Rickettsia* species, and *F. tularensis;* the result was confirmed by Western blot. The patient's eschar and lymphadenopathy resolved after 6 weeks of treatment with doxycycline. No alopecia at the eschar site was observed

Discussion. In this report, we identified 3 patients with SENLAT who seroconverted to *B. henselae* and 1 patient with negative IFA and positive Western blot results after a tick bite. Serum samples negative by IFA and positive by Western blot can be observed during the onset of the disease [8]. On the basis of molecular methods, we confirmed that the eschar biopsy specimens from 2 of the patients also contained DNA of *B. henselae* and that an attached *Dermacentor* tick form one of the patients contained DNA of *B. henselae*. Each of the patients with SENLAT were bitten by ticks during colder months, consistent with activity of *Dermacentor* ticks in Europe and with the observation that SENLAT cases are not recorded during the warmest summer months [4]. From these data we believe that *B. henselae* is likely the cause of these 3 cases of SENLAT.

R. slovaca and *R. raoultii* have been detected in or isolated from *Dermacentor* ticks in Eurasia, which inhabit forests and pastures, and frequently bite people, particularly on the scalp [4]. During recent years, molecular epidemiology surveys throughout the world suggest that ticks are competent vectors of *Bartonella* species [9]. The presence of *Bartonella* species, in most cases, has been identified using PCR analysis using primers targeting either specific *Bartonella* genes or the 16S rDNA gene and results revealed that the proportion of ticks harboring *Bartonella* DNA is variable [9]. However, only Kruszewska and Tylewska-Wiezbanowska [10] achieved the isolation of *Bartonella* species from a tick. Direct proof of transmission of *Bartonella* species by a tick was reported by Noguchi in 1926, who described experimental transmission of *Bartonella bacilliformis* to monkeys by *Dermacentor andersoni*. Recently, Cotté

et al [11] published a report detailing the potential transmission of *B. henselae* by *Ixodes ricinus* ticks in an experimental model. Ticks have long been considered a potential source of *B. henselae* infection based on epidemiological evidence [9]; however, this topic is still subject of discussion. Transmission of *B. henselae* from a tick to a human host has not yet been proved, and only circumstantial evidence of tick transmission has been reported [9].

SENLAT is a common clinical entity that occurs most frequently in women and children during the colder months and is caused by *R. slovaca, R. raoultii,* and possibly also *B. burgdorferi* [2]. We believe that the designations "TIBOLA" and "DEBONEL," which were proposed initially for this clinical entity, are not inclusive of the growing number of infectious agents causing a scalp eschar and neck lymphadenopathy following tick bite. We propose a new name of this syndrome (SENLAT) that is independent of a specific etiologic agent, and we have found that the spectrum of the causative agents of SENLAT should be extended. Other agents of SENLAT may also exist, because in many cases (25% in this series), the causative agent remains undetermined. The report and others [12] indicate that the clinical spectrum caused by *B. henselae* continues to expand.

Acknowledgments

We are grateful to Christopher D. Paddock for critical reading and for English revisions of this manuscript.

Potential conflicts of interest. All authors: no conflicts.

References

1. Raoult D, Lakos A, Fenollar F, Beytout J, Brouqui P, Fournier PE. Spotless rickettsiosis caused by *Rickettsia slovaca* and associated with *Dermacentor* ticks. Clin Infect Dis **2002**; 34:1331–1336.
2. Lakos A. Tick-borne lymphadenopathy (TIBOLA). Wien Klin Wochenschr **2002**; 114:648–654.
3. Ibarra V, Oteo JA, Portillo A, et al. *Rickettsia slovaca* infection: DEBONEL/TIBOLA. Ann N Y Acad Sci **2006**; 1078:206–214.
4. Parola P, Rovery C, Rolain JM, Brouqui P, Davoust B, Raoult D. *Dermacentor* borne rickettsioses (TIBOLA/DEBONEL): the role of *Rickettsia slovaca* and *R. raoultii*. Emerg Infect Dis **2009**; 15:1105–1108.
5. Angelakis E, Roux V, Raoult D, Rolain JM. Real-time PCR strategy and detection of bacterial agents of lymphadenitis. Eur J Clin Microbiol Infect Dis **2009**; 28:1363–1368.
6. Socolovschi C, Matsumoto K, Brouqui P, Raoult D, Parola P. Experimental infection of *Rhipicephalus sanguineus* with *Rickettsia conorii conorii*. Clin Microbiol Infect **2009**.
7. Raoult D, Roblot F, Rolain JM, et al. First isolation of *Bartonella alsatica* from a valve of a patient with endocarditis. J Clin Microbiol **2006**; 44: 278–279.
8. Maurin M, Rolain JM, Raoult D. Comparison of in-house and commercial slides for detection of immunoglobulins G and M by immunofluorescence against *Bartonella henselae* and *Bartonella quintana*. Clin Diag Lab Immunol **2002**; 9:1004–1009.
9. Angelakis E, Billeter SA, Breitschwerdt EB, Chomel B, Raoult D. Are there tick-borne Bartonelloses? Emerg Infect Dis (in press).
10. Kruszewska D, Tylewska-Wierzbanowska S. Unknown species of rickettsiae isolated from ixodes riconus tick in Walcz. Roczniki Akademii Medycznej w Bialymstoku **1996**; 41:129–135.
11. Cotte V, Bonnet S, Le-Rhun D., et al. Transmission of *Bartonella henselae* by *Ixodes ricinus*. Emerg Infect Dis **2008**; 14:1074–1080.
12. Raoult D. From Cat scratch disease to *Bartonella henselae* infection. Clin Infect Dis **2007**; 45:1541–1542.