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### Travel Medicine and Infectious Disease

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#### Rickettsia massiliae infection after a tick bite on the eyelid

Dear Editor, we read with interest the paper [1] describing diverse rickettsial infections in Croatia and would like to describe a case of *Rickettsia massiliae* infection and highlight previously reported cases of this unusual infection.

A 61-year-old woman, was bitten by a tick on her right eyelid while walking in a wooded area a few kilometres from Bologna, Italy. She removed the tick the day after the bite and after four days she developed an erythematous lesion on her right eyelid and latero-cervical satellite lymphadenopathy. She also developed occipital headache with painful neck, low grade fever, general malaise, asthenia and generalized joint pain. She was examined by a general practitioner and an ophthalmologist. Amoxicillin/clavulanate 875/125 mg q12h and ofloxacin eye drops therapy was started, with no benefit.

Because of the persistence of symptoms, she went to the A&E department of Sant'Orsola-Malpighi Hospital in Bologna. Blood examinations, brain CT scan and chest X-ray were normal. Doxycycline was started and the dosing interval of amoxicilline/clavulanate was increased for a total duration of 15 and 21 days respectively. She had fever, occipital headaches, severe asthenia, low-grade hip and knees arthralgia for an additional 4–5 days, with progressive clinical resolution. At the last clinical visit, the patient's overall condition was good: she had a complete resolution of symptoms except mild asthenia.

Biopsy and swab of the eyelid lesion were sent to the reference center for rickettsial diseseases in Marseille, France. DNA was extracted from skin biopsy and swab using the EZ1 Advanced XL (Qiagen, German) biorobot and the DNA tissue kit. In-house specific real-time qPCR targeting all the spotted fever group *Rickettsia*, and 3 qPCR specifically targeting *R. conorii*, *R. mongolitimonae* and *R. massiliae* were performed using primers and probes previously described [2]. The qPCRs for the spotted fever Rickettsia group and *R. massiliae* were positive with Ct value at 33 and 27 respectively. Specific qPCR for *R. conorii* and *R. mongolitimonae* were negative. qPCR was positive for *R. massiliae* with 37 Ct value on the swab sample.

*R. massiliae* was first isolated in 1990 in a tick (*Rhipicephalus tur-anicus*) in southern France and described in 1993 as a new spotted fever group *Rickettsia* [3]. Then, it has been found in *Rhipicephalus spp* ticks in Europe, Africa and America [4,5]. It is a good example of a bacteria identified in ticks several years before its involvement in human diseases.

To date, eight human cases of *R. massiliae* infection have been reported (Table 1). In 2006, Vitale et *al.* [6] obtained the first human isolate from a patient presenting with spotted fever. Almost all cases have been reported from the Mediterranean region, except one in a Spanish traveler returning from Argentina (Table 1). Clinical presentation is mostly the one of a spotted fever rickettsiosis with eschar inoculation, fever and rash, that can be purpuric [7]. However, one case of SENLAT (Scalp Eschar and Neck Lymphadenopathy After Tick bite) has also been reported (Table 1). In our present case, the clinical presentation is close to that of a SENLAT, but with an atypical eschar site in the eyelid, mimicking Meibomian cyst. It adds new data about the clinical manifestations of *R. massiliae* infection. This observation is in line with previous studies suggesting that SENLAT is not a pathogen-specific reaction [8].

qPCR on a cutaneous swab specimen of the eschar detected *R. massiliae.* The use of swab for the diagnosis of rickettsia is less invasive, especially in atypical localization where cutaneous biopsy can be difficult [9]. In our case, both the biopsy sample and swab sample were positive, again demonstrating that the swab sampling is a sensitive technique.

To date, no case of *R. massiliae* infection had a fatal outcome. *R. massiliae*, similarly to *Rickettsia aeschlimannii*, has a natural resistance to rifampicin, which is associated with a different *rpoB* sequence than other rickettsiae [6]. The therapeutic strategy is the same as recommended for all tick-borne rickettsioses [9]: prompt doxycycline treatment should be initiated in case of clinical suspicion.

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Table 1   Human cases of R. n	<i>tassiliae</i> infe	ction.						
Cases	Country	Sex, Age	Co morbidities	Clinical presentation	Clinical syndrome	Microbiological identification	Treatment	Outcomes
Vitale et al., 2006	Sicilia	M, 45	n. k.	Fever, Rash, Eschar, Hepatomegaly	Spotted fever	Cell Culture and PCR from blood	Tetracycline	Cured
Parola et al., 2008	France	M, 25	None	Fever, Eschar $(\times 2)$ , Rash, Acute vision loss	Spotted fever Bilateral Chorioretinitis	PCR (cutaneous biopsy, aqueous humor)	Doxycycline, Ofloxacin and Glucocorticoid (IV)	Ophthalmic sequelae
Garcia et al., 2009	Argentina*	W, 56	Seizure, Arteriovenous Malformation	Fever, Purpuric rash Eschar	Spotted fever	PCR (cutaneous biopsy)	Doxycycline (12 days)	Cured
Cascio et al., 2013	Sicilia	M, 13	None	Headache, Fever, Cervical Lymphadenitis. Eschar. Hepatomegaly	SENLAT	PCR (cutaneous biopsy)	Doxycycline	Cured
Zaharia et al. 2016	Romania	M, 76 W 49	Not Known	Fever, Rash, conjunctivitis, Myalgia, Eschar Eever Rash Myaloia Fechar	Spotted fever	Western Blot with Cross Absorption	Doxycycline (7 days)	Cured
Chochlakis et al., 2016	Greece	M, 62	None	Fever, twont, myangaa, myangaa, eschar, Fever, headache, myalgia, eschar, upper extremities rash	Spotted fever	IFA	Doxycycline (14 days)	Cured
Khrouf et al., 2016	Tunisia	Not Known	Not Known	Fever, rash, eschar	Spotted fever	PCR on skin biopsy	Not Known	Not Known
SENLAT: Scalp Esch *: imported case in ( IFA: Indirect Immun	ar and Lymp Spain. ofluo rescen	hadenopathy ce Assay.	After Tick bite.					

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