

Koralur et al. 69

in motor power of all four limbs was seen, with simultaneous emergence of deep tendon reflexes. By the tenth day, ventilator support was weaned.

At the time of discharge, free ambulation with the help of a walker was possible. Four weeks later at outpatient review, he had regained full motor power in all four limbs and had no remaining signs and symptoms of his recent neurotoxicity.

#### Discussion

Neurological manifestations may result from envenomation from the *elapidae* group snakes such as cobra and krait. Snake bite is an occupational hazard for farmers or labourers working in open fields or forests and for people sleeping in the open. A high index of suspicion is required in such cases, as in most instances a definite history of snake bite is absent and the bite marks are not visible.

LIS is a rare neurological condition where complete paralysis of voluntary muscles occurs except those of the eye; cognition remains intact.

Bauer described three types of locked in states: (1) total, with complete quadriplegia with anarthria; (2) classic, similar to total, but with preserved vertical eye movements and consciousness; and (3) incomplete, similar to classic, with some voluntary movements present along with eye movements.<sup>2</sup>

Common causes of LIS are polyneuropathy, toxins, myasthenia gravis, encephalitis, stroke and trauma.<sup>3</sup>

LIS from snake envenomation occurs as a result of neuromuscular transmission blockade at the peripheral level from post-synaptical binding at acetylcholine receptors in cobra bites or pre-synaptical binding, preventing acetylcholine release, in krait bites. Only very few such cases have been reported in the literature. 5–7

LIS can readily be misdiagnosed as brain death; slow recovery may add to this misinterpretation. The use of anti-venom therapy and ventilator almost always results in complete recovery with no residual neurological deficit in LIS.

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#### References

- Kalantri S, Singh A, Joshi R, et al. Clinical predictors of in-hospital mortality in patients with snake bite: a retrospective study from a rural hospital in central India. *Trop Med Int Health* 2006; 11: 22–30.
- Bauer G, Gerstenbrand F and Rumpl E. Varieties of locked-in syndrome. J Neurol 1979; 221: 77–91.
- Smith E and Delargy M. Locked-in syndrome. BMJ 2005; 330: 406–409.
- 4. Warrell DA and International Panel of Experts. Guidelines for the clinical management of snake bite in the South-East Asia region. *Southeast Asian J Trop Med Public Health* 1999; 30(Suppl.): 11–85.
- 5. Prakash S, Mathew C and Bhagat S. Locked-in syndrome in snakebite. *J Assoc Physic India* 2008; 56: 121–122.
- Azad C, Mahajan V and Jat RK. Locked in syndrome as presentation in snake bite. *Indian Pediatr* 2013; 50: 695–697.
- Varadarajan P, Sankaralingam T and Sangareddy SPJ. Peripheral locked in syndrome following snake envenomation. *Pediatric Oncall* 2013; 10: 41. Available at: http://www.pediatriconcall.com/pediatric-journal/View/FullText-Articles/570/J/0/0/28/0
- 8. John J, Gane BD, Plakkal N, et al. Snake bite mimicking brain death. *Cases J* 2008; 1: 16.

### Scrub typhus reinfection

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70 Tropical Doctor 48(1)

**Table 1.** Comparison of symptoms and laboratory results from the two episodes of ST infection.

	Second admission (2015)	First admission (2014)
Fever	Present	Present
Occupation	Supervising agricultural work only	Active agricultural work
Headache	Present	Absent
Headache	Present	Absent
Abdominal pain	Absent	Present
Eschar	Absent	Present
Oedema	Pedal odema and facial puffiness present	Facial puffiness present
Other significant findings		
Dyspnoea	Present	Present
Vesicular lesions	Present	Absent
N-PCR (blood)	Positive	Positive
IFA	Positive (1:128)	Positive (1:128)
IgM ELISA	Positive	Positive
Weil–Felix test (OX-K) ≥ 1:160	Negative	Positive (1:640)

#### **Keywords**

Scrub typhus, reinfection, India, tsutsugamushi, absence of eschar

#### Introduction

Scrub typhus (ST), a mite-borne rickettsial disease, has increased in frequency in India, among other countries, in recent years. 1,2 It is most commonly characterised as a febrile disease with a range of varying symptoms. This disseminated multi-organ disease may be lifethreatening if not treated early during the illness and relapses with early cessation of treatment are common.<sup>3</sup> Approximately 1 million ST cases occur annually, although surveillance statistics are poor in many countries. However, potentially > 1 billion people are at the risk of infection.<sup>4</sup> The chigger vectors themselves act as the disease reservoirs and man is an accidental host. Agriculturalists residing in and travellers visiting the endemic area (the tsutsugamushi triangle) during activities such as rafting, hiking and trekking are at the greatest risk of the disease.<sup>5</sup> Outbreaks of ST in military units are common,<sup>6</sup> such as a recent outbreak during the Cowley beach exercise in Australia. Mortality rates were high in the pre-antibiotic era; decreasing mortality has been seen in recent years.8,9 Broad antigenic heterogeneity is observed in *Orientia tsutsugamushi* (OT),<sup>8</sup> and thus vaccines have not yet been successfully developed. Newer endemic areas have been identified in China. 10 New evidence from Kenya and Chile indicates a larger endemic zone of ST than was previously believed to have existed, although this may be due to unrecognised species. 11,12 Unresolved problems associated with ST include: pathogenesis; diagnosis and prognosis; and the role of immunity. Research progress in reducing the burden of this disease has been slow.<sup>13</sup> Early vaccine trials have shown that resistance to reinfection with homologous strains may occur up to three years and immunity to heterologous strains seem to dissipate within two years. 14 It is believed that reinfection with OT is relatively common in high endemic areas, although cell-mediated immunity may play an important role in recovery. 15,16 Because of this, reinfections are rarely detected. Here we report a patient with ST who was infected twice in consecutive years confirmed by both laboratory tests and positive clinical recovery with anti-rickettsial antibiotics during both episodes. Our report also emphasises the possibility of reinfection in ST which may present with different clinical manifestations between episodes, including the possible absence of an eschar.

#### Case report

In September 2015, a 58-year-old agriculturalist presented to Kasturba Hospital, Manipal, Karnataka with high-grade continuous fever associated with rigors of eight days' duration and frontal headache for seven days. On examination, his vital parameters were normal and systemic examination was unremarkable. Mild bilateral pitting pedal oedema with facial puffiness was noticeable. A thorough physical

Koralur et al. 71

examination failed to identify an eschar. Vesicular lesions were incidentally noticed over the right angle of the mouth, for which the patient was successfully treated with topical acyclovir. He had not travelled elsewhere, but had been admitted and treated for a ST infection in the previous year and had refrained from active agricultural activity since then. Laboratory results showed a normal white cell count  $(8.1 \times 10^9)$ L), a high erythrocyte sedimentation rate (ESR; and thrombocytopenia  $(115 \times 10^9/L)$ . Dengue, Weil-Felix test (OX-K, OX-2 and OX19) and malaria testing were negative. An ultrasound scan of the abdomen was normal. Serum antibodies to OT were positive by M-IFA and ST IgM ELISA.<sup>17</sup> The nested polymerase chain reaction (N-PCR) performed on DNA from the buffy coat was positive with a 483-bp product after amplifying with primers specific for the 56-kDa TSA. 18 Doxycycline 100 mg twice daily on the day of admission was administered. Platelet counts steadily normalised and the patient was discharged six days after admission as he was asymptomatic. Incidentally, during admission, he had complained of dyspnoea on exertion; an ECG showed T-wave inversion, which was treated solely with aspirin.

During late July 2014, the same patient was admitted with the chief complaint of dyspnoea on exertion for a period of two weeks. He had mild bilateral pitting oedema with facial puffiness, an eschar with a scab that had fallen off in the left lumbar region, and with mild tenderness in both right and left lumbar regions. Laboratory results showed leucocytosis  $(15.6 \times 10^9/L)$ , an elevated ESR level (52 mm/h), normal platelet counts  $(280 \times 10^9/L)$  and an elevated creatinine level (129.6 µmol/L). The Weil-Felix test for (OX-K) antigen (1:640), ST IgM Micro immunofluorescence assay (M-IFA) and ST IgM ELISA were positive. N-PCR with STA56 gene primers with DNA from the buffy coat was also positive confirming the diagnosis as ST.18 Doxycycline 100 mg twice daily was administered empirically as ST was suspected on the first day of admission. Improvement was seen and the patient was discharged after five days, being asymptomatic again.

Table 1 provides a summary comparison of symptoms and laboratory results between the two episodes. Antibodies to OX-K were not observed in the second episode of illness in this case, even after nine days of febrile illness, a finding consistent with a response to reinfection. However, IgM was detected by ELISA and this is usually absent or delayed (Table 1).<sup>15</sup>

#### **Discussion**

ST is primarily a rural disease and those exposed to infective chiggers are at the greatest risk. ST

reinfections are known to occur in endemic regions, but are rarely reported. 15,16 The present case was an agriculturalist by occupation and was more active during the initial episode rather than the latter. Following the initial episode, he only supervised the work undertaken when he visited agricultural farms. Recently, large numbers of ST cases have been observed from the area where our patient was working; ST is more common during the cooler months of the vear. Human immunity from the first infection may last for one to three years against the homologous strain but is short-lived (less than one year) against the heterologous strains. 19 In our case, reinfection occurred 14 months later, during which time the immunity generated had waned, especially if the infecting strain was of heterologous type. Interestingly, during the second episode, our patient did not present with an eschar. Experimental studies suggested that an eschar was more closely associated with primary infection than reinfection. 14 Thus, immunity from the primary infection may only be sufficient to prevent the formation of an eschar but not avoid active infection. Phylogenetic analysis of infective strains may provide more information on this point.

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#### References

- Wu Y-C, Qian Q, Magalhaes RJS, et al. Rapid increase in scrub typhus incidence in mainland China, 2006–2014.
   Am J Trop Med Hyg 2016; 94: 532–536.
- 2. Luce-Fedrow A, Mullins K, Kostik AP, et al. Strategies for detecting rickettsiae and diagnosing rickettsial diseases. *Future Microbiol* 2015; 10: 537–564.
- Im JH, Baek JH, Lee JS, et al. In vitro bacteriostatic effects of rifampin on Orientia tsutsugamushi. *J Korean Med Sci* 2014; 29: 183–189.
- Richards AL. Worldwide detection and identification of new and old rickettsiae and rickettsial diseases. FEMS Immunol Med Microbiol 2012; 64: 107–110.

72 Tropical Doctor 48(1)

 Liu Q and Panpanich R. Antibiotics for treating scrub typhus (Review). Cochrane Database Syst Rev 2010; 23: CD002150.

- Kelly DJ, Richards AL, Temenak J, et al. The past and present threat of rickettsial diseases to military medicine and international public health. *Clin Infect Dis* 2002; 34: S145–169.
- Harris PN, Oltvolgyi C, Islam A, et al. An outbreak of scrub typhus in military personnel despite protocols for antibiotic prophylaxis: Doxycycline resistance excluded by a quantitative PCR-based susceptibility assay. *Microbes Infection* 2016; 18: 406–411.
- Kelly DJ, Fuerst PA, Ching WM, et al. Scrub typhus: the geographic distribution of phenotypic and genotypic variants of Orientia tsutsugamushi. *Clin Infect Dis* 2009; 48(Suppl. 3): S203–230.
- 9. Varghese GM, Trowbridge P, Janardhanan J, et al. Clinical profile and improving mortality trend of scrub typhus in South India. *Int J Infect Dis* 2014; 23: 39–43.
- 10. Zhang S, Song H, Liu Y, et al. Scrub typhus in previously unrecognized areas of endemicity in China. *J Clin Microbiol* 2010; 48: 1241–1244.
- 11. Thiga JW, Mutai BK, Eyako WK, et al. High seroprevalence of antibodies against spotted fever and scrub typhus bacteria in patients with febrile Illness, Kenya. *Emerg Infect Dis* 2015; 21: 688–691.
- Kharod G, Person M, Folkema A, et al. Uganda National Acute Febrile Illness Agent Detection Serosurvey 2004–2005. Int J Infect Dis 2016; 45: 180.

- Paris DH, Shelite TR, Day NP, et al. Unresolved problems related to scrub typhus: a seriously neglected lifethreatening disease. Am J Trop Med Hyg 2013; 89: 301–307.
- 14. Smadel JE, Ley HL Jr, Diercks FH, et al. Immunization against scrub typhus: duration of immunity in volunteers following combined living vaccine and chemoprophylaxis. *Am J Trop Med Hyg* 1952; 1: 87–99.
- 15. Bourgeois AL, Olson JG, Fang RC, et al. Humoral and cellular responses in scrub typhus patients reflecting primary infection and reinfection with Rickettsia tsutsugamushi. *Am J Trop Med Hyg* 1982; 31: 532–540.
- Ching WM, Rowland D, Zhang Z, et al. Early diagnosis of scrub typhus with a rapid flow assay using recombinant major outer membrane protein antigen (r56) of Orientia tsutsugamushi. Clin Diagn Lab Immunol 2001; 8: 409–414.
- 17. Koraluru M, Bairy I, Varma M, et al. Diagnostic validation of selected serological tests for detecting scrub typhus. *Microbiol Immunol* 2015; 59: 371–374.
- Furuya Y, Yoshida Y, Katayama T, et al. Serotype-specific amplification of Rickettsia tsutsugamushi DNA by nested polymerase chain reaction. *J Clin Microbiol* 1993; 31: 1637–1640.
- 19. Stover CK, Marana DP, Dasch GA, et al. Molecular cloning and sequence analysis of the Sta58 major antigen gene of Rickettsia tsutsugamushi: sequence homology and antigenic comparison of Sta58 to the 60-kilodalton family of stress proteins. *Infect Immun* 1990; 58: 1360–1368.

# Leprosy case detection campaign (LCDC) for active surveillance

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## Pugazhenthan Thangaraju<sup>1</sup>, Sajitha Venkatesan<sup>1</sup> and MK Showkath Ali<sup>2</sup>

We read with great interest a case report published in your journal entitled 'Conjugal leprosy: is there a need for active surveillance in endemic areas?' Here, we try to add some additional points pertaining to this case and information regarding the active surveillance that is being carried out in the endemic and non-endemic areas by the Government of India Central Leprosy Division.

The authors have emphasised the prevalence of conjugal leprosy, with either of the partners being the index case. We feel that the clinical spectrum in both members occurred in the same period of time. In the manuscript, it was mentioned that the man had consulted seven months prior for weakness of the right foot and

that clinical examination had revealed a right foot drop with sensory loss; his wife had symptoms pertaining to leprosy for the past year before she reported with her husband.

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