Research letter

Out of Sight, Top of Mind: A Pediatric Traveler's Hidden Scalp Eschar and its Implications for Scrub Typhus Exposure in Western Thailand.

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Scrub typhus in pediatric travelers is seldom reported. Here, we describe an untypical presentation of scrub typhus in an 8-year-old Asian-Caucasian boy who traveled to a national park in Southern Thailand. He exhibited fever symptoms with chills, headache, cervical and occipital lymphadenopathy, and a painless scalp eschar discovered five days after fever onset. Blood and eschar PCR confirmed the presence of *O. tsutsugamushi* infection, and treatment with doxycycline led to prompt resolution of symptoms. This case highlights the importance of considering scrub typhus in febrile child travelers, recognizing atypical eschar locations for diagnosis, and understanding the diagnostic implications.

Scrub typhus is transmitted by mites from the Trombiculidae family, specifically the *Leptotrombidium* genus, during their larval (chigger) stage. These chiggers latch onto hosts to feed on lysed skin cells and serve as both the vector and reservoir for the bacterium *Orientia Tsutsugamushi*. They can transmit this bacterium both transovarially (from mother to offspring) and transstadially (between different stages of their lifecycle) [1]. Due to their diminutive size, chigger bites are often painless and easily go unnoticed by the host.

Case report. An 8-year-old, previously healthy Asian-Caucasian boy presented at a travel clinic with a three-day history of fever, chills, headache, and loss of appetite. The patient had recently traveled to Kaeng Krachan National Park on the Thailand-Myanmar border approximately two

weeks prior to presentation. While there, he partook in outdoor excursions such as bird watching, wildlife viewing, and day and night hiking up to an elevation of 974 meters. On examination on the third day of fever, the patient was alert, febrile (37.9 °C), and hemodynamically stable. Physical examination revealed right cervical lymphadenopathy, an enlarged right occipital lymph node, and multiple insect bite lesions on the lower legs. Additionally, the parent reported that the child's intermittent fevers were accompanied by bilateral headache. Despite a thorough examination, no eschar was identified.

Initial laboratory findings showed mild leukocytosis with left shift and mild transaminitis (WBC 4.4×10 μ/L, neutrophil 60%, lymphocyte 21%, band 5%, atypical lymphocyte 1%, platelets 133×10^3 μ/L, AST 48 U/L, ALT 32 U/L). Tests for dengue NS1 antigen and malaria films were negative. Given the limitations of conventional tests for ruling out rickettsial infection and other bacterial infections, blood was sent for multiplex real-time PCR targeting for *Leptospira* species (16S rDNA), *Rickettsia* species (gltA gene), *O. tsutsugamushi* (16S rDNA) and Eubacteria (16S rDNA).

PCR results became available two days after the initial presentation. The PCR targeting the 16S rRNA gene to *O. tsutsugamushi* showed equivocal signals. Thus, an additional real-time PCR targeting the 47-kDa protein yielded positive results. Molecular assays for other microorganisms were negative. Coincidentally, on this same day, the child identified a small, painless eschar on the scalp, measuring 3 mm x 3 mm, as depicted in Figure 1. The targeted PCR for the 47-kDa protein on the eschar sample confirmed an *O. tsutsugamushi* infection. Indirect immunofluorescent antibody assay (IFA) against *O. tsutsugamushi* was negative (titer <10) on day 5 but later became positive on day 9 (IgM titer 1:100) and day 24 (IgG titer 1:40) post-fever onset (Supplementary File 1). Comparison of longitudinal IgG and IgM antibody responses on IFA, ELISA and InBios scrub typhus rapid test are shown in Figure 2. The child had an IgM response on IFA, ELISA, and rapid test between 5 and 9 days after fever onset and an IgG response 20 days after. IgM responses measured using IFA and ELISA peaked at 17 days after fever onset. Both IgM and IgG responses remained positive on the rapid test for 59 days after fever onset.

Oral administration of 100 mg doxycycline twice daily was prescribed. The fever alleviated within 36 hours; however, the child remained weak for two weeks. The eschar lesion disappeared after 3 weeks from symptom onset.

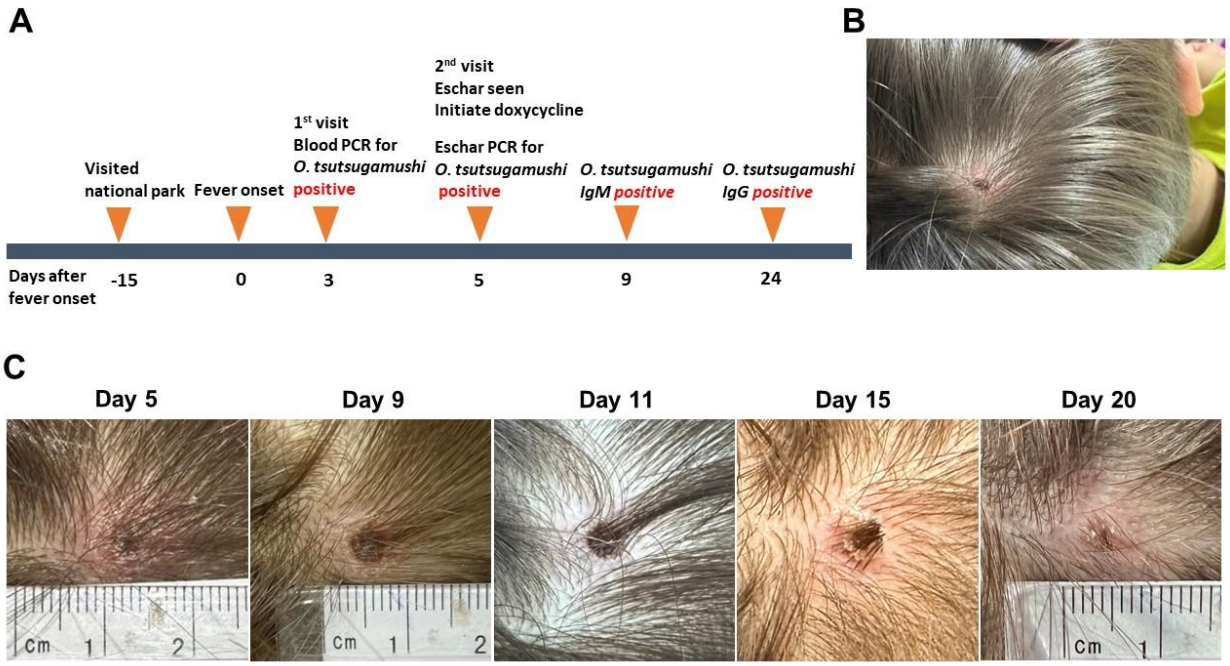

Figure 1: A) Timeline representing main events, B) Eschar lesion on the scalp (5 days after fever onset), C) Evolution of eschar progression and number of days after fever onset.

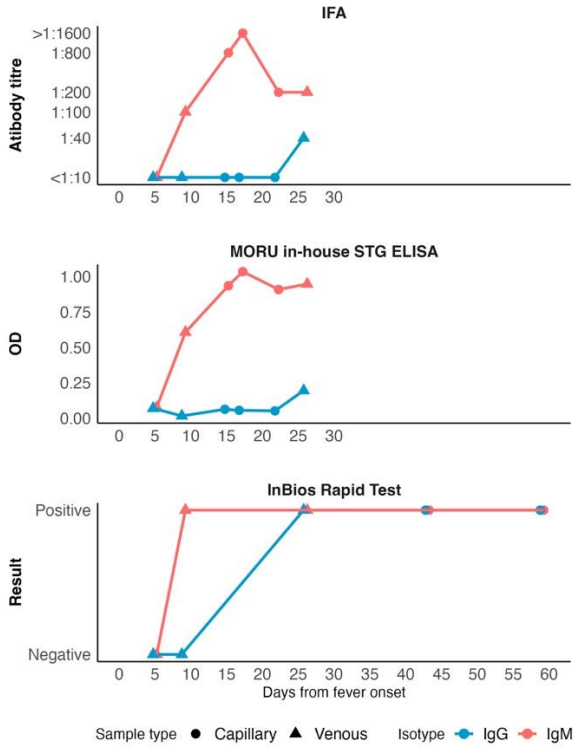

Figure 2: Longitudinal IgM and IgG responses using IFA, MORU in-house scrub typhus ELISA and InBios Rapid Test following scrub typhus infection.

Discussion. This report presents a case of scrub typhus in a pediatric traveler with an atypical eschar site. In low-resource settings where diagnostics tests are limited, the presence of eschar becomes a crucial clue in diagnosing scrub typhus. A systematic review reported an overall eschar detection of 58%, with variation across geographical regions [2]. In adults, the eschars were more frequently observed in the lower parts of the body [3]. For children, the presence of eschar was documented at 40.8%, with the most common sites being the groin and axilla areas. Head and neck areas were also common sites for eschar in children, accounting for 19.1% of detection [3]. However, most head and neck lesions were located on the ear and neck, scalp lesions were extremely rare [3]. Children's smaller stature may increase the likelihood that chiggers reach their scalp to bite. Additionally, eschars on the scalp can be easily overlooked due to concealment by hair. The presence of an occipital lymph node might indicate the need for a thorough examination of the scalp for hidden eschars.

While the IFA is traditionally recognized as the gold standard for diagnosing scrub typhus, it proved inconclusive during the early stage of the disease. Samples collected at 5 days after fever

onset tested negative for IgM and IgG. A four-fold rise in antibody titers was observed about one week after fever onset, highlighting the potential delay in treatment while waiting for serology results. This delay also applies when using in-house ELISA tests and InBios rapid tests, which similarly were not positive until sometime between 5 and 9 days after fever onset. Severe complications of pediatric scrub typhus include bronchopneumonia, meningoencephalitis and hemophagocytic lymphohistiocytosis, delayed treatment can increase the likelihood these sever complications [4]. Interestingly, the 16S PCR conducted on whole blood 3 days post-symptom onset exhibited a high Cq value of 41.6 (Cut-off value 40) and could have been overlooked without additional targeted PCR performed. By the 5th day after symptom onset, the PCR analysis on both the buffy coat sample and eschar confirmed the diagnosis of *O. tsutsugamushi* infection. The availability of affordable multiplex PCR for bacterial pathogens would be invaluable for early identification and ensuring timely, appropriate treatment, particularly when an eschar is absent. Furthermore, maintaining a high index of suspicion for rickettsial infection is essential when encountering patients with acute undifferentiated fever engaged in outdoor activities during Thailand's rainy season (June to November) [5].

Scrub typhus is rarely reported in travelers, with approximately forty cases documented [6]. Predominantly, higher risk activities among travelers in Southeast Asia are associated with outdoor activities like trekking [7]. Kaeng Krachan National Park, located at the border of Myanmar, is the largest national park in Thailand, covering about 2900 km² [8] with elevations reaching 1,500 meters above sea level [8]. It is popular among both international and domestic travelers, providing ample opportunities for trekking, wildlife, and bird watching. To our knowledge, no known cases have been described from travelers to this park. Moreover, reports of endemic transmission in this region of Thailand are scarce. As ecotourism activities grow, the trend of scrub typhus in non-local people may increase. Physicians should be aware of the potential for scrub typhus infections among both domestic and international travelers visiting this region of Thailand.

We present a rare case of scrub typhus in a child traveler and highlight the diagnostic challenges and implications. The subtle nature of eschar, which can go unnoticed, underscores the need for meticulous clinical examination, particularly in less common areas such as the scalp. The presence of occipital lymphadenopathy may serve as a clinical clue for potential scalp eschars. In the early stages of scrub typhus, eschar plays a pivotal role before a measurable antibody response develops.

Accurate and affordable diagnostic options such as multiplex PCR are urgently required for acute infections prior to the development of antibody responses. Moreover, when evaluating patients returning from rural areas of Thailand with acute undifferentiated fever and a history of ecotourism activities, scrub typhus should be considered as part of differential diagnosis.

Conflict of interest

None to declare.

Author contribution

P.L, W.M., and S.C. conceptualized the idea, P.L., W.M., and S.C. developed the initial manuscript draft. P.L., W.M., S.C., K.A., J.J., J.W., S.D.B. and A.R., critically revised and edited the manuscript. All authors read and approved the final manuscript.

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Data Availability

The data underlying this article will be shared on reasonable request to the corresponding author.

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