



Letter to the Editor

Scrub typhus with urinary tract infection and leukopenia: A case series

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Dear Editor:

Scrub typhus is a mite-borne disease caused by *Orientia tsutsugamushi*. The common manifestations of scrub typhus include fever, pneumonia, liver dysfunction, and acute kidney injury [1]. Leukopenia and urinary tract infection (UTI) caused by *O. tsutsugamushi* have rarely been reported. Herein, we reported four scrub typhus cases presenting as UTIs with leukopenia in Shandong Province, China.

Case 1. A 67-year-old man presented to the hospital claiming fever, fatigue, muscle soreness, and cough. Enlarged lymph nodes in the groin and skin lesion produced by arthropod bite was observed. Laboratory results showed bronchitis, leukopenia, hematuria, and proteinuria, with the urine WBC (white blood cell) and RBC (red blood cell) counts being 19 and 89, respectively. Elevated AST (glutamic oxaloacetic transaminase), ALT (glutamic-pyruvic transaminase), and LDH (lactate dehydrogenase) were also observed (Table 1). He was suspected infected with severe fever with thrombocytopenia syndrome virus (SFTSV) or *Brucella* sp., then favipiravir and doxycycline were applied. However, subsequent tests were negative for both. On the 12th day, the symptoms were relieved and he left the hospital.

Case 2. A 70-year-old woman was admitted with fever, dizziness, fatigue, and muscle soreness for 26 days. Arthropod-bite lesion was recorded and skin rash was observed on the back, hip, and inner thigh. Laboratory results revealed leukopenia, hematuria, and proteinuria, with the urine WBC and RBC counts being 63 and 72, respectively. She was clinically diagnosed with rickettsial infection, invasive pulmonary aspergillosis, and septic shock. Meropenem, voriconazole, and doxycycline were applied. Since the 13th day, her laboratory indicators returned to normal. She left the hospital on the 15th day.

Case 3. A 50-year-old woman complaint fever, malaise, headache, chill, anorexia, joint soreness, throat dryness, and nausea for 7 days. Skin lesion, conjunctival congestion, and enlarged tonsils were also described. Hematuria, and proteinuria were indicated by urinalysis, with the urine WBC and RBC counts being 66 and 32, respectively. Routine blood tests also indicated leukopenia, thrombocytopenia, elevated PCT, and elevated LDH. Viral infection was suspected.

Favipiravir and piperacillin tazobactam were used. Additionally, granulocyte colony-stimulating factor was applied to increase the WBC. On the 5th day, her body temperature became normal, and she was set free from the hospital.

Case 4. A 77-year-old woman was admitted with fever, fatigue, palpitation, and nausea. Arthropod-bite skin lesion was observed. Routine blood tests showed leukopenia, thrombocytopenia, elevated PCT, ALT, AST, and LDH. Meanwhile, laboratory data also showed hematuria, and proteinuria, with the urine WBC and RBC counts being 74 and 307, respectively. SFTSV infection and viral encephalitis were suspected. Favipiravir and ceftriaxone were applied for antiviral and antibacterial therapy. Glycerin fructose, albumin, and furosemide were also used for supportive treatment. On the 6th day, she was transferred to the ICU. However, the symptoms still worsened. On the 9th day, the patient gave up treatment and left the hospital.

In a retrospective study, the serum samples of the patients were collected to screen for vector-borne pathogens. Immunofluorescence assay (IFA) test using an *O. tsutsugamushi* IFA IgG/IgM Kit (Fuller, USA) showed that all four cases were positive for *O. tsutsugamushi*. Recent or active infections were confirmed for cases 1, 2, and 3 (IgG titers of $\geq 1:512$, or IgM titers of $\geq 1:64$), while case 4 was infected at an undermined time (IgG titers of $\geq 1:128$) (Table 1 and Figure 1). No other vector-borne pathogens were detected.

In this study, all four patients showed some symptoms in common: Hematuria, proteinuria, and increases in urinary WBC and RBC (except for the urinary WBC of Case 1), suggesting UTIs which has been rarely reported in these patients. In 2021, Liu et al. has reported a scrub typhus case presenting as a UTI [2]. As was previously reported, *O. tsutsugamushi* replicates in the vascular endothelium and mononuclear macrophages of humans, thus affecting almost all organs including the urinary system [3]. We suspect that this may be the mechanism of scrub typhus-associated UTIs. Leukopenia has been considered a criterion to differentiate SFTS against scrub typhus [4,5]. In our study, all four patients showed leukopenia, suggesting that leukopenia might be common in certain populations/areas and it might not always be a suitable criterion to differentiate scrub typhus and SFTS.

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Table 1

Results of laboratory tests of the five patients on admission day and the retrospective serological test results.

	Reference Value	Case 1	Case 2	Case 3	Case 4
Age		67	70	50	77
Gender		male	female	female	female
Blood test					
RBC (10 ⁹ /L)	4.3–5.8 (male) 3.0–5.0 (female)	3.98	2.55	4.08	3.73
WBC (10 ⁹ /L)	4–10	1.37	2.68	2.00	2.10
PLT (10 ⁹ /L)	125–350	28	110	90	53
PCT (ng/mL)	0–0.05	0.224	0.061	0.092	2.33
ALT (IU/L)	9–50	403	29	48	100
AST (IU/L)	15–40	228	53	45	53
LDH (IU/L)	120–250	930	447	380	566
Urinalysis					
Urine Protein	– (negative)	+3	+-	+1	+2
Urine Occult Blood	– (negative)	+2	+2	+-	+3
Urine WBC Count	0–28	19	63	66	74
Urine RBC Count	0–17	89	72	32	307
IgG titer		1:512	1:128	1:512	1:128
IgM titer		–	1:64	–	–

Abbreviations: RBC, red blood cell; WBC, white blood cell; PLT, platelet; PCT, procalcitonin; ALT, glutamic-pyruvic transaminase; AST, glutamic oxaloacetic transaminase; LDH, lactate dehydrogenase.

CRedit authorship contribution statement

Cuiping Wu: Data curation, Project administration, Resources. **Miao Lu:** Investigation, Methodology. **Xuejun Dong:** Data curation, Resources. **Yitong Jiang:** Investigation. **Bo Liang:** Data curation, Resources. **Kun Li:** Conceptualization, Data curation, Writing – original draft, Writing – review & editing.

Ethical approval statement

This work was approved by the Ethic Committee of Weifang Yidu Central Hospital.

Consent for publication

Not applicable.

Availability of data and material

Not applicable.

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Declaration of competing interest

All authors declare no conflict of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.nmni.2024.101548>.

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