Scrub typhus as a rare cause of acute pyelonephritis: case report

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Abstract

Background: Scrub typhus can present with atypical signs and symptoms such as those of acute kidney injury, gastroenteritis, pneumonitis, and acute respiratory distress syndrome. Meningitis, encephalitis, and hepatic dysfunction have also been reported, particularly in severe cases with multisystem involvement. Scrub typhus has never been reported in the literature to cause urinary tract infections (UTIs) which includes cystitis and pyelonephritis.

Case presentation: A 45-year old male presenting to the outpatient unit with fever, right flank pain, and burning micturition for three days was initially treated for UTI. However, he returned to the hospital on the fourth day of illness with persistent symptoms. He was hospitalized, with intravenous (IV) ceftriaxone. Computerized tomography scan of his abdomen-pelvis showed features of acute pyelonephritis, so his antibiotics were upgraded to meropenem and teicoplanin. Despite this, the patient’s condition deteriorated. Laboratory investigations showed multisystem involvement: decreasing platelets, raised creatinine, and deranged liver panel. As Kathmandu was hit by dengue epidemic during the patient’s hospitalization, on the seventh day of his illness, blood samples were sent for tropical fever investigation. All tests came out negative except for scrub typhus—IgM antibodies positive on rapid diagnostic test. The patient’s symptoms subsided after 48 h of starting doxycycline and he became fully asymptomatic four days later. Fever did not recur even after discontinuing other IV antibiotics, favoring scrub typhus disease rather than systemic bacterial sepsis.

Conclusions: Scrub typhus is an emerging infectious disease of Nepal. Therefore, every unexplained fever cases (irrespective of clinical presentation) should be evaluated for potential Rickettsiosis. Moreover, for cases with acute pyelonephritis, atypical causative agents should be investigated, for example scrub typhus in this case.

Keywords: Scrub typhus, Acute pyelonephritis, Urinary tract infection, Case report

Background

Scrub typhus is a mite-borne infectious disease caused by a bacteria called Orientia tsutsugamushi, previously known as Rickettsia tsutsugamushi [1]. It is one of the emerging infectious diseases of Nepal [2]. Clinical manifestation of scrub typhus includes a painless papule called eschar representing localized cutaneous necrosis at the site of infecting chigger bite, followed by fever, generalized headache, diffuse myalgia, anorexia, generalized lymphadenopathy, and non-pruritic body rash. However, it can present with atypical signs and symptoms such as those of acute kidney injury, gastroenteritis, rarely pneumonitis, and acute respiratory distress syndrome. Meningitis, encephalitis, and hepatic dysfunction have been reported too, particularly in severe cases, with multisystem involvement [3]. Case fatality rate of scrub typhus is 6% for untreated and 1.4% for treated cases [1]. [4] Therefore, a high degree of clinical suspicion is required for the diagnosis of scrub typhus which can be confirmed by a rapid diagnostic test or
Pyelonephritis can develop if pathogens ascend to the vertebral angle tenderness, and pelvic or perineal pain. with chills or rigors, fatigue or malaise, flank pain, costovertebral angle tenderness, and pelvic or perineal pain. Patients with UTI present with fever and occasionally with persistent symptoms. He was then admitted to the medical ward with intravenous (IV) ceftriaxone 1 g twice daily, injection tramadol for pain, and intravenous fluids. Serum creatinine level increased to 1.5 mg/dL whereas blood urea (30 mg/dL), sodium (135 mmol/L), and potassium (3.8 mmol/L) levels decreased. Liver panel (transaminases, total and direct bilirubin, alkaline phosphate, serum lipase, serum amylase) was normal. (Table 1).

The patient continued to be symptomatic on Day 5 of illness despite IV medication. Routine urine and blood investigations came out unremarkable except for a sudden decrease in platelet count (190,000 on Day 4 to 115,000 on Day 5) and serum creatinine level (1.5 on Day 4 to 1.3 on Day 5). (Table 1) Follow-up US abdomen-pelvis showed globular right kidney with probe tenderness, suggestive of acute pyelonephritis. Antibiotics were then upgraded to IV meropenem and IV teicoplanin.

A plain computer tomography scan of the patient’s kidneys-ureters-bladder (CT-KUB) showed right perirenal haziness and fatty strandings; thickened right lateral renal fascia with minimal surrounding haziness but no evidence of hydroureteronephrosis; tiny renal concretions, splenunculus, and plateatelectasis in the posterobasal segment of right lower lobe of right kidney; and mild degenerative changes in the visualized spine. These findings complemented the US diagnosis of acute pyelonephritis. (Fig. 1).

On Day 7 of illness, the patient was still complaining right flank pain along with fever. He suddenly became tachypneic with respiratory rate of 24/min. An urgent US chest was performed which showed minimal bilateral pleural effusion. Routine laboratory investigations came out unremarkable except for decreasing creatinine level (1.2 mg/dL). (Table 1) Then, a possibility of serositis was suspected.

Kathmandu city was hit by dengue epidemic at the time of the patient’s hospital admission. Therefore, a possibility of tropical fever in this patient was thought of too. His blood samples were sent for the investigation for dengue virus, scrub typhus, leptospirosis, leishmaniasis (kala-azar), and malaria (optimal test). All tests came out negative except for scrub typhus – IgM antibodies positive on rapid diagnostic test. Immediately, doxycycline (100 mg IV twice daily) was added to the patient’s medication list (Day 7 of illness).

The patient’s clinical features and lab results did not change remarkably for 36 h of initiating doxycycline. However, over the next 48 h (Day 10 onwards), the patient showed clinical improvement. His fever and abdominal pain decreased significantly. On Day 12 of illness (9th day of admission, 7th day of IV meropenem, 5th day of IV doxycycline), the patient had a feeling of well-being, so he was sent home with oral doxycycline for 10 additional days and oral levofloxacin for 7 days.
When the patient visited hospital after 6 days of discharge (Day 17), he was found apparently asymptomatic; all blood and urine investigations came out normal; and his follow-up ultrasonography findings (chest-abdomen-pelvis) were non-significant.

**Discussion and conclusions**
Renal abnormalities in scrub typhus case range from proteinuria or hematuria to acute kidney injury and occasionally chronic kidney disease [8]. Acute pyelonephritis in scrub typhus has been reported only once in the

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**Table 1** Laboratory investigation timeline and reports (abnormal values are marked in bold)

| Laboratory parameters | Normal values (KMC Lab protocol) | Day 1 | Day 4 | Day 5 | Day 6 | Day 7 (Doxycycline added) | Day 8 | Day 10 | Day 17 |
|-----------------------|----------------------------------|------|------|------|------|---------------------------|------|-------|-------|
| **Hematology**        |                                  |      |      |      |      |                           |      |       |       |
| TC (cells/mm³)        | 3500-10,500                      | 10,700 | 14,800 | 12,200 | 11,100 | 11,400                    | 12,500 | 12,400 | 7400  |
| DC (%)                | N60-80, L20-30, E1-4             | N82  | N66  | N83 L15 | N87  | N80                       | N71 L27 | N73 L22 | N67 L26 |
| Hb (gm/dL)            | 12–16                            | 13.4 | 13.7 | 11.0  | 10.8  | 10.4                      | 11.2  | 10.7  | 11.7  |
| Platelets (cells/mm³) | 150,000-450,000                  | 192,000 | 190,000 | 115,000 | 120,000 | 145,000                  | 212,000 | 232,000 | 490,000 |
| ESR (mm/hr)           | < 15                             | 41   |      |       |       |                           |      |       |       |
| **Renal panel**       |                                  |      |      |      |      |                           |      |       |       |
| Urea (mg/dL)          | 15–45                            | 29   | 30   | 25    | 22    | 29                        | 18   | 33    | 33    |
| Creatinine (mg/dL)    | 0.5–1.2                          | 1.0  | 1.5  | 1.3   | 1.2   | 1.2                       | 1.0  | 1.0   | 0.9   |
| Sodium (mmol/L)       | 135–145                          | 138  | 135  | 136   | 136   | 136                       | 138  | 138   | 142   |
| Potassium (mmol/L)    | 3.5–5.0                          | 3.7  | 3.8  | 3.8   | 3.4   | 3.1                       | 3.5  | 3.5   | 4.8   |
| **Liver panel**       |                                  |      |      |      |      |                           |      |       |       |
| Total Bilirubin mg/dL | 0.2–1.2                          | 1.7  |      |       |       |                           |      |       |       |
| Direct Bilirubin (mg/dL) | 0–0.4                       | 1.0  |      |       |       |                           |      |       |       |
| SGPT/SGOT (IU/L)      | < 45 each                        | 32/16 |      |       |       |                           |      |       |       |
| ALP (IU/L)            | 50–100                           | 521  |      |       |       |                           |      |       |       |
| Albumin (gm/dL)       | 3.5–5.0                          |      |      |       |       |                           |      |       |       |
| PT/INR (sec)          | 11.0–13.5/15.0/1.17              |      |      |       |       |                           |      |       |       |
|                       | 0.8–1.2                           |      |      |       |       |                           |      |       |       |
| **Urine examination** |                                  |      |      |       |       |                           |      |       |       |
| Urine pus cells (per hpf) | < 1–2   | 10–12 | plenty | 0–2 |      |                           |      |       |       |
| Urine RBC             | nil                               | nil  | nil  | nil   |      |                           |      |       |       |
| Urine albumin         | nil                               | nil  | nil  | nil   |      |                           |      |       |       |
| Urine culture         | no growth                         | no growth | no growth |      |       |                           |      |       |       |
| **Other blood tests** |                                  |      |      |       |       |                           |      |       |       |
| Random sugar (mg/dL)  | 60–140                           | 99   |      |       |       |                           |      |       |       |
| Serum Lipase/Amylase (U/L) | 10–160/25 | 15/25 |      |       |       |                           |      |       |       |
| Blood culture         | no growth                         |      |      |       |       |                           |      |       |       |
| **Tropical panel serology** |                    |      |      |       |       |                           |      |       |       |
| Scrub typhus          | positive (rapid IgM)              |      |      |       |       |                           |      |       |       |
| Leptospira            | negative                          |      |      |       |       |                           |      |       |       |
| Dengue                | negative                          |      |      |       |       |                           |      |       |       |
| Leishmaniasis         | negative                          |      |      |       |       |                           |      |       |       |
| Malaria (optimal test)| negative                          |      |      |       |       |                           |      |       |       |
literature—in a 56-year-old Chinese lady who presented with frequent micturition, flank pain, and an eschar in her body [9]. The mechanisms postulated for renal involvement include typhus-related vasculitis, tubular interstitial proliferation, and tubular necrosis [8].

In the current case, poor control of symptoms with oral and intravenous antibiotics (cefixime, ceftriaxone, meropenem and teicoplanin), abnormal laboratory and radiographic reports suggestive of multiorgan involvement (decreasing platelet counts, decreasing creatinine, deranged liver panel, globular right kidney, bilateral pleural effusion), and an ongoing tropical fever epidemic in Kathmandu prompted the clinicians to investigate for an atypical causative agent.

Positive rapid serological test (IgM antibodies against scrub typhus) confirmed the diagnosis. All investigation reports including US chest-abdomen-pelvis drastically came out normal, with no evidence of pyelonephritis, after 10 days of initiating doxycycline (Day 17 of onset of illness). Moreover, patient’s fever did not recur even after discontinuing other intravenous antibiotics, favoring scrub typhus disease rather than systemic bacterial sepsis.

Acute febrile illness can present with atypical clinical signs and symptoms, often with multisystem involvement, that should urge clinicians to look for atypical pathogens—for example scrub typhus associated with pyelonephritis in this case. Scrub typhus is a common but neglected tropical disease in South Asia including Nepal. Therefore, stakeholders should not wait until an outbreak or epidemic occurs to initiate standard surveillance programs, deploy reliable and affordable diagnostic kits at all levels of healthcare service, and raise community awareness about disease transmission and preventative measures.

Abbreviations
ALP: Alkaline phosphatase; CT: Computerized tomography; DC: Differential count; ESR: Erythrocyte sedimentation rate; Hb: Hemoglobin; IFA: Immunofluorescence assay; KMC: Kathmandu medical college; KUB: Kidneys-ureters-bladder; PCR: Polymerase chain reaction; PT/INR: Prothrombin time/International normalized ratio; SGPT/SGOT: Serum glutamic pyruvic transaminase/oxaloacetic transaminase; TLC: Total leucocyte count; UTI: Urinary tract infection

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Authors’ contributions
TB, SCP, and NP were involved in patient treatment. TB and NP collected samples and laboratory reports. SB supervised the study. TB and SB interpreted test results, and wrote the first manuscript draft. All authors reviewed and approved the final version of manuscript.

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Availability of data and materials
All the information supporting our conclusions and relevant references are included in the manuscript. There are no datasets related to this case report.
Ethics approval and consent to participate
Institutional ethical approval is generally not required for case reports in our setting. The patient provided informed consent in written form to participate in this study.

Consent for publication
The patient authorized the main author, in written form, to publish this case report and the accompanying image (CT KUB). A copy of the consent is available for review by the journal editor.

Competing interests
All authors declare that they have no competing interests.

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