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Nephrology

Acute Kidney Injury Secondary to Rickettsiosis: A Four-Case Series from Morocco and Literature Review

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Abstract | **Case Report**

Background: Rickettsial infections are zoonoses caused by Rickettsia species, transmitted mainly by ticks and fleas. While usually mild, they may occasionally lead to severe visceral involvement, including acute kidney injury (AKI). ***Methods***: We report four cases of rickettsial infection complicated by AKI in Morocco, detailing clinical, laboratory, and radiological features, and review the recent literature. ***Results*:** All patients presented with fever and generalized rash, with varying gastrointestinal symptoms and multi-organ involvement. Laboratory findings included AKI, thrombocytopenia, elevated inflammatory markers, and hepatic cytolysis. Rickettsial serology was unavailable in all cases. Early treatment with doxycycline and supportive therapy led to rapid clinical and biological recovery. ***Conclusion*:** AKI can complicate rickettsial infections. Early clinical recognition and prompt doxycycline therapy are associated with favorable outcomes, even in the absence of confirmatory serology.

Keywords: Rickettsiosis, Acute Kidney Injury, Epidemiology, Doxycycline Treatment.

INTRODUCTION

Rickettsiosis is a zoonotic infection caused by bacteria of the genus Rickettsia, primarily transmitted through arthropod vectors such as ticks and fleas. Rickettsial diseases are endemic in Mediterranean and tropical regions, where cases are commonly associated with contact with infected animals, particularly dogs [1, 2]. Although rickettsiosis typically presents as a febrile illness accompanied by a cutaneous rash, severe visceral involvement may occur and has been documented in clinical case series [3, 4]. Among these complications, acute kidney injury (AKI) is uncommon but represents a poor prognostic factor when present [3-5].

Early recognition of rickettsiosis and its potential complications is crucial for prompt management and favorable outcomes. However, reports of AKI secondary to rickettsial infection remain scarce in the literature, particularly in North Africa [2, 3]. Therefore, presenting detailed clinical, biological, and therapeutic data from such cases can provide valuable insights for clinicians working in endemic areas.

In this context, we report a series of four cases of rickettsiosis complicated by AKI in Morocco, aiming to illustrate the spectrum of clinical presentations, highlight diagnostic challenges, and discuss the impact of early therapeutic intervention.

CASE REPORTS

Case 1

A 53-year-old Moroccan man presented with a 10-day history of high-grade fever (39°C), vomiting, and watery diarrhea, followed by the appearance of a generalized non-pruritic maculopapular rash involving the palms and soles, associated with palatal enanthem. Physical examination revealed mild dehydration and a necrotic inoculation eschar on the right buttock (Figure 1-A).

Laboratory investigations demonstrated leukocytosis (10,700/mm³), thrombocytopenia (120,000/mm³), elevated C-reactive protein (256 mg/L), hepatic cytolysis, hyponatremia (130 mEq/L), and acute kidney injury with serum creatinine of 1017 µmol/L, along with mild proteinuria. Blood and urine cultures were sterile, and rickettsial serology was unavailable.

Given the epidemiological exposure (contact with dogs), characteristic rash, and presence of an eschar, a diagnosis of Mediterranean spotted fever complicated by acute kidney injury was retained. The patient was treated with doxycycline 100 mg twice daily for 7–10 days along with intravenous rehydration, resulting in rapid clinical improvement and complete recovery of renal function within three weeks.

Case 2

An 83-year-old male patient was admitted for febrile illness associated with a diffuse maculopapular eruption. A tick was found attached to the thoracic region without a visible inoculation eschar (Figure 1-B). Biological workup revealed acute kidney injury with a serum creatinine of 168 µmol/L, severe hyponatremia (125 mEq/L), thrombocytopenia (103,000/mm³), leukocytosis, elevated CRP (163 mg/L), and hepatic cytolysis. Urinalysis showed mild proteinuria, while imaging studies were unremarkable. In the context of tick exposure in an endemic area, rickettsiosis complicated by renal involvement was strongly suspected despite the absence of serological confirmation. The patient received doxycycline (100 mg twice daily for 7 days) combined with intravenous fluids, leading to rapid clinical and biological recovery.

Case 3

A 61-year-old shepherd, with frequent exposure to dogs, presented with moderate fever (38°C) and a diffuse maculopapular rash. Clinical examination identified an inoculation eschar in the sub-umbilical region (Figure 1-C).

Laboratory findings showed leukocytosis (12,000/mm³), elevated CRP (67 mg/L), hyponatremia (129 mEq/L), hepatic cytolysis, and acute kidney injury with a serum creatinine of 195 µmol/L, associated with mild proteinuria. Imaging was unremarkable, and serological testing was not available. Considering the occupational exposure, clinical presentation, and presence of an eschar, rickettsial infection complicated by acute kidney injury was diagnosed. Treatment with doxycycline and intravenous hydration resulted in rapid resolution of symptoms and normalization of laboratory abnormalities.

Case 4

A 60-year-old farmer with significant exposure to dogs presented with acute onset of high fever (39°C), vomiting, and diarrhea. Dermatological examination revealed an extensive maculopapular rash involving the trunk and extremities (Figure 1-D and E).

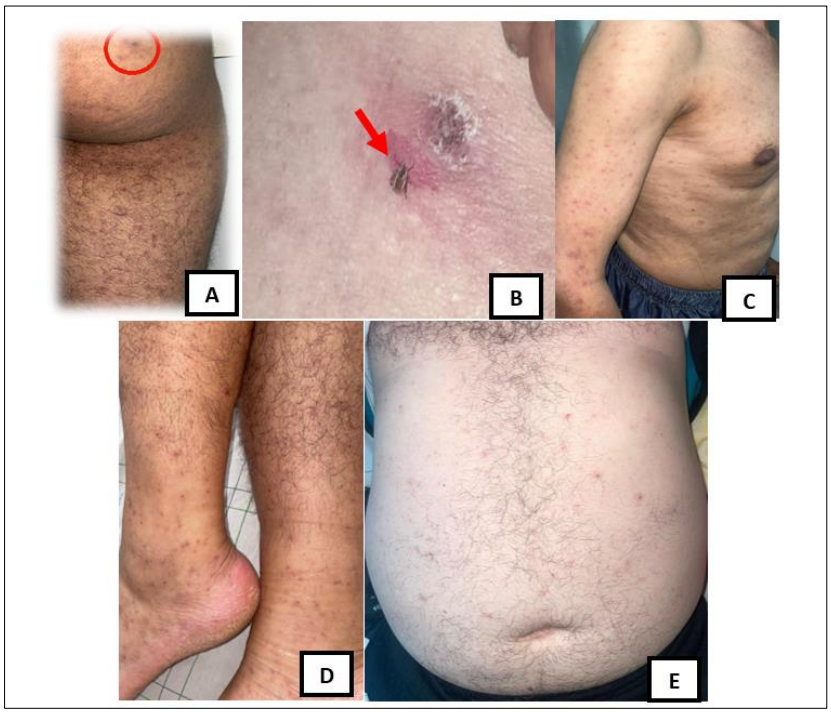

Figure 1: Representative cutaneous manifestations of rickettsiosis in our patient
A – Inoculation eschar (black necrotic spot) on the right buttock, outlined with a red circle.
B – Red arrow indicating the presence of a rickettsial tick on the thorax.
C – Maculopapular rash involving the trunk and upper limbs.
D – Maculopapular rash affecting the lower limbs.
E – Generalized maculopapular rash on the abdomen.

Laboratory evaluation showed leukocytosis (13,000/mm³), thrombocytopenia (124,000/mm³), markedly elevated CRP (264 mg/L), hepatic cytolysis, and acute kidney injury with a serum creatinine of 174 µmol/L. Proteinuria was significant (1.35 g/day). Imaging studies were normal. In this endemic context

with multiorgan involvement, Mediterranean spotted fever complicated by acute renal impairment was diagnosed. The patient was treated with doxycycline (100 mg twice daily for 10 days) and intravenous rehydration, resulting in rapid clinical improvement and complete normalization of renal function and inflammatory markers within one week.

Overall, the four patients presented with acute febrile illness associated with generalized maculopapular rash in an endemic Moroccan setting. Epidemiological exposure was identified in all cases, either through close contact with dogs or direct tick attachment, and an inoculation eschar was observed in two patients. Acute kidney injury was present in all cases, accompanied by mild proteinuria. Thrombocytopenia, elevated inflammatory markers, hepatic cytolysis, and hyponatremia were frequent associated findings, reflecting multi-organ involvement. Rickettsial serology was unavailable in all patients ; therefore, diagnosis was based on clinical and epidemiological arguments. All patients received doxycycline (100 mg twice daily) with intravenous rehydration, resulting in rapid clinical improvement and complete recovery of renal function, without the need for renal replacement therapy (Table 1)

Table 1: Comparative characteristics of the four patients

Variable	Case 1	Case 2	Case 3	Case 4
Age (years)	53	83	61	60
Sex	Male	Male	Male	Male
Epidemiological exposure	Dog contact	Tick attached	Dog contact	Dog contact
Inoculation eschar	Yes	No	Yes	No
Fever	Yes (39°C)	Yes (38°C)	Yes (38°C)	Yes (39°C)
Rash	Generalized, palmo-plantar	Generalized	Generalized	Generalized
Gastrointestinal symptoms	Yes	No	Mild diarrhea	Yes
Leukocytosis	Yes	Yes	Yes	Yes
Thrombocytopenia	Yes	Yes	No	Yes
Hyponatremia	Yes	Yes	Yes	No
Hepatic cytolysis	Yes	Yes	Yes	Yes
Peak creatinine (µmol/L)	1017	168	195	174
Proteinuria	0.34 g/day	0.38 g /day	0.40 g /day	1.35 g/day
Outcome	Complete recovery	Complete recovery	Complete recovery	Complete recovery

DISCUSSION

Mediterranean spotted fever (MSF), caused by Rickettsia conorii subspecies conorii, is the predominant tick-borne rickettsial disease in the Mediterranean basin and remains endemic in North Africa and surrounding regions [1]. MSF is transmitted primarily by the brown dog tick Rhipicephalus sanguineus, and the classical association of febrile exanthema with an inoculation eschar in endemic regions should raise clinical suspicion for rickettsial infection [2].

All four patients in this series were hospitalized during the summer months, consistent with the well-described seasonality of MSF. Epidemiological studies have shown that cases cluster seasonally during warmer months — typically between May and October — when tick activity increases and transmission risk is highest [1-4]. Although this pattern is well established, sporadic cases occurring outside the classic peak have also been documented [1].

In North Africa, including Morocco and neighboring Maghreb countries, the distribution, prevalence, and vector ecology of rickettsial diseases remain incompletely characterized due to limited surveillance and underreporting. Recent regional analyses confirm that Rickettsia conorii remains the most frequently encountered species, particularly in Tunisia and Algeria, with high incidence rates reported in multiple clinical series [4, 1].

The increasing visibility of MSF in surveillance data likely reflects a combination of ecological, climatic, and socio-demographic changes, including urban expansion into rural areas, increased contact between humans and domestic animals, and climate influences on vector populations [4]. Contact with dogs — a common host for Rhipicephalus sanguineus — has been repeatedly identified as a significant epidemiological factor [1-4]. In our series, direct tick attachment was documented in one patient, supporting this association.

MSF affects all age groups, although some data suggest a male predominance and increased risk among individuals with occupational or environmental exposure to ticks [1]. Early symptoms of rickettsial infection are non-specific, which may lead to delayed diagnosis. Serological testing, particularly indirect immunofluorescence assay (IFA), remains the reference standard but has limitations due to delayed seroconversion, often making early diagnosis reliant on clinical and epidemiological features rather than laboratory confirmation [6]. Although MSF typically presents with fever and rash, diffuse visceral

involvement — including neurological, hepatic, and renal complications — occurs in a minority of cases. Acute kidney injury is an uncommon but increasingly recognized complication, particularly in severe presentations that involve systemic inflammation and endothelial dysfunction [5-7].

Several mechanisms may contribute to renal impairment in MSF, including hypovolemia from gastrointestinal fluid losses, microvascular endothelial injury, and systemic cytokine effects leading to increased vascular permeability with consequent reduced renal perfusion. If left untreated, these processes can progress to ischemic tubular injury and acute tubular necrosis [5-7]. Hyponatremia has also been observed in rickettsial infections, often due to increased antidiuretic hormone (ADH) secretion in response to hypovolemia and inflammation. Studies document significant sodium decreases in patients with severe MSF, highlighting the importance of careful electrolyte monitoring [8].

Although rare, severe MSF with pathologically confirmed renal histological injury, including acute tubular necrosis and crescentic glomerulonephritis, has been documented and may progress to end-stage renal disease in untreated cases [9]. In contrast, the AKI observed in our patients appeared predominantly functional, with rapid reversal following appropriate fluid resuscitation and doxycycline therapy. This aligns with international case reports demonstrating reversibility of AKI when treatment is initiated promptly [3-10].

Doxycycline remains the first-line therapy for MSF and other rickettsial infections, with recommended dosing of 200 mg per day for 7–10 days. In severe cases or where oral administration is not feasible, alternative agents such as fluoroquinolones may be considered, though evidence supports doxycycline's continued central role in management [6, 7]. In our series, all patients responded favorably to oral doxycycline with complete resolution of symptoms and renal function recovery.

Conclusion

This work has increased our clinical vigilance, highlighting the need to consider rickettsial infection in any patient presenting with acute kidney injury accompanied by a generalized febrile rash, particularly when epidemiological risk factors are present. Diagnosis should not delay the initiation of treatment, which is essential to prevent progression to severe disease.

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