

## Case Report

# Isolated third nerve palsy complicating rickettsial infection: A rare neurological complication

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## Introduction

Rickettsial infections are important re-emerging zoonotic infections, worldwide. They are caused by a heterogenous group of obligate intracellular Gram negative cocobacilli belonging to the family *Rickettsiaceae*. The genus *Rickettsia* encompasses the rickettsiae responsible for causing spotted fevers [i.e. the spotted fever group (SFG)] and the rickettsiae responsible for causing typhus (the typhus group) while the genus *Orientia* contains only *Orientia tsutsugamushi* which causes scrub typhus [1]. Rickettsioses usually present as a febrile illness and can have a myriad of complications. Neurological complications, although rare, are well described in the literature. We report a patient with isolated third nerve palsy complicating rickettsial infection.

## Case Report

A 72-year-old, previously well patient from Hatton presented with fever of six days duration. She had noticed a generalized, non-pruritic, erythematous rash, together with arthralgia and myalgia, following the onset of fever. Two days into the illness she developed progressive drooping of the left eye lid and diplopia. There was no diurnal variation, ocular pain or redness. There was no history of vomiting, photophobia or severe headache. She did not complain of any other focal neurological weakness, numbness or clouding of consciousness. She was mainly living indoors and there was no history of tick bite or possible tick exposures.

On examination, she was febrile with a temperature of 102 °C. There was no pallor, icterus or lymphadenopathy. A careful examination failed to demonstrate an eschar. She had a generalized, erythematous, maculopapular rash, more prominent on the lower limbs and back of the chest [Figure 1]. Neurological examination was remarkable for a left side complete ptosis with medial gaze restriction [Figure 2]. The left pupil was slightly dilated and was only sluggishly reactive to light. The right eye and the rest of the neurological examination were normal. There were no signs of meningeal irritation and other system examinations were also unremarkable.

Full blood count showed a total leucocyte count of  $9 \times 10^9/L$  with haemoglobin 12.5 g/dL and platelet  $345 \times 10^9/L$ . Erythrocyte sedimentation rate was 45mm/1<sup>st</sup> hour and C reactive protein level was 51.5 mg/dL. Blood cultures and urine cultures did not yield any growth. Contrast enhanced CT scan of the brain, including orbital cuts, were normal as was the arteriogram and venogram of the cerebral vessels. Cerebrospinal fluid examination was normal with a protein content of 40mg/dL and three lymphocytes/ $\mu L$ . Skin biopsy revealed superficial cutaneous vasculitis. Antinuclear factor, rheumatoid factor, C and P ANCA were negative. Retroviral screening was negative and VDRL was non-reactive. The Weil-Felix test demonstrated a significant positive titre of 1:320 for OX19.



Figure 1: Generalized erythematous maculopapular rash



Figure 2: Left sided complete ptosis

She was treated for rickettsial infection with intravenous ceftriaxone for four days followed by a course of oral doxycycline. There was a dramatic clinical improvement with defervescence and disappearance of the rash. The third nerve palsy was present on discharge. However, by the one-month review it was remarkably improved.

### Discussion

The typical clinical picture of rickettsiosis comprises of high fever, headache and a characteristic skin rash. Duration of disease is about two to three weeks and the severity may range from a mild febrile illness to a fatal disease with multi organ failure. The rash can be maculopapular, vesicular, purpuric or, in severe cases, necrotic and gangrenous. The rash is a result of a vasculitis, attributed to the proliferation of rickettsiae in the endothelium of cutaneous vessels or toxin mediated damage. An eschar may be evident in some patients indicating the site of the tick bite [1].

A study carried out in the Central Province identified three types of rickettsioses, namely scrub typhus, spotted fever and murine typhus [2]. However, in our patient, subtyping was not feasible due to the unavailability of resources. In that study, a correlation was observed between OX 19 positivity in the Weil-Felix test and antibodies against *R. typhi* by indirect fluorescent antibody testing, although it was not strong enough to recommend the use of the Weil-Felix test for definitive diagnosis of this subtype. The Weil-Felix test is based on the detection of antibodies against *Proteus* species that cross react with bacteria of the genus *Rickettsia*. OX 19 positivity is seen in patients infected with the typhus group and in Rocky Mountain spotted fever. Due to the advent of more accurate diagnostic tests, the Weil-Felix test is currently only used in resource poor settings [3].

Rickettsioses can result in diverse neurological complications. In a Sri Lankan case series of spotted fever group rickettsioses, neurological sequelae comprised altered level of consciousness, extrapyramidal signs including tremor, rigidity and dyskinesia, weakness of limbs including a rare case of flaccid quadriplegia and two cases of deafness [4]. Meningoencephalitis leading to fatal and nonfatal sequelae are well described in the international literature [5,6].

Cranial nerve involvement in rickettsioses has been seldom reported in the literature, which indicates its rarity. Facial nerve palsy, vestibulocochlear nerve palsy, abducens palsy and a single case of isolated third nerve palsy have been reported [7,8,9,10,11]. A series of lower motor facial nerve palsy due to intra-aural tick bites with associated rickettsial infection has been reported in Sri Lanka [12].

The pathological hallmark of rickettsial infection is vasculitis; resulting in microvascular leakage, oedema, endothelial damage, microthrombi formation and resultant end organ hypoperfusion with ischaemic injury [13]. Neurological disease is similarly attributed to vascular inflammation causing meningoencephalitis, which may result in focal deficits. However, cranial nerve palsies occurring in the absence of clinical, laboratory or imaging evidence of meningoencephalitis, are thought to be a consequence of selective vasculitis affecting the respective nerves. A necropsy study has demonstrated focal grey and white matter necrosis in a case of neuro-rickettsiosis and another study has shown foci of cerebral vasculitis with mononuclear cell infiltrates involving the blood vessels and the perivascular space [14,15].

Available therapies for rickettsioses include tetracyclines (mainly doxycycline), chloramphenicol, macrolides and fluoroquinolones. Steroids have been used in neurological disease but their efficacy and utility is yet to be formally established. Most patients have recovered uneventfully. Nonetheless fatalities and permanent disabilities are well documented in the literature.

## Conclusion

Rickettsioses are important emerging infections in Sri Lanka. Neurological sequelae are significant complications. As isolated cranial nerve palsy is a rare presentation of this disease, a rickettsial aetiology may be overlooked in such cases. A careful history and a thorough examination, together with a high clinical suspicion and awareness about rare

forms of presentation, are cornerstones in the diagnosis. Appropriate and timely treatment will prevent fatal and irreversible complications.

### Consent

Informed written consent was obtained from the patient for publication of this case report and for all accompanying images.

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