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Case Report

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Rickettsioses complicated with dry gangrene and thrombotic thrombocytopenic purpura -a case report

Abstract

Background: Spotted fever group rickettsioses has become more apparent in certain provinces of Sri Lanka. It has a vast diversity in its clinical presentation. However, toe gangrene and thrombotic thrombocytopenic purpura are rare presentations of rickettsioses and are less reported to date.

Case presentation: Acute febrile illness of a 28year old Army Officer was complicated with seizures, acute kidney injury, toe gangrene and skin necrosis. He was treated as for spotted fever group rickettsioses complicated with dry gangrene and thrombotic thrombocytopenic purpura. Accurate clinical diagnosis and specific treatment resulted in dramatic recovery leaving behind only the residual gangrenous toes.

Conclusion: This case report highlights the importance of accurate clinical diagnosis along with timely intervention to determine the outcome of certain detrimental and rare complications of spotted fever group rickettsioses.

Keywords: rickettsioses, dry gangrene, thrombotic thrombocytopenic purpura, case report

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Introduction

The rickettsiae are a heterogenous group of small, obligately intracellular gram negative coccobacilli and short bacilli which are transmitted by ticks, mites, fleas or lice acting as vectors. Clinical infections can be classified according to the taxonomy, epidemiology and clinical manifestations. Studies have shown that there are different types of rickettsial infections in the central province of Sri Lanka of which Orientia tsutsugamushi, Rickettsia typhi and spotted fever group are the identified types.[1] The clinical picture may range from a mild illness to a detrimental multi organ dysfunction. Cutaneous lesions play a major role in supporting the diagnosis which may present as a maculopapular rash, eschar, vasculitic rash or fern leaf necrosis when severe.[2] Gangrene of the digits or whole limb; which is an uncommon complication; has been commonly reported with Rocky Mountain Spotted Fever. Small vessel occlusion is the proposed explanation for the digital gangrene.[3,4] Also, thrombotic thrombocytopenic purpura is another very uncommon complication which is less reported as a consequence of rickettsioses.[5]. Many cases go unnoticed due to lack of diagnostic technology, therefore a high index of clinical suspicion and clinical awareness is essential and early prompt treatment is necessary. We present this young soldier who developed some rare clinical manifestations of rickettsial infection.

Clinical presentation

This previously well 28 year old army officer from Mawanella had presented to the local hospital with fever, headache, arthralgia and myalgia for six days. He has had no photophobia, vomiting, upper or lower respiratory tract or urinary symptoms. He denies any chronic sinusitis or recent onset bronchial asthma. The usual source of water had been the river nearby from which he bathes daily. He gives no history of his neighbors being treated for a similar type of fever as for dengue or leptospirosis or typhus. He was a smoker and consumed cannabis occasionally and only an occasional drinker. He had consumed cannabis only four months ago; denies any other drugs especially being administered in the form of injections or any high risk behaviours or tattooing. He had been found to have only low platelets at the local hospital along with free fluid in the hepatorenal pouch. Initially he had been managed as for dengue hemorrhagic fever. There had been a further drop in platelets with an acute kidney injury. He was then intubated due to several episodes of generalized tonic clonic seizures with deteriorating levels of consciousness. Subsequently, he was transferred for ICU care at National Hospital Kandy.

He had been hemodynamically stable but febrile on admission to local hospital. He has had no signs of meningeal irritation. There had been no visible eschar. The following day (day 8 of illness) after being admitted to the Medical Intensive Care Unit (ICU) at Teaching Hospital Kandy he was found to have the typical fern leaf pattern rash of rickettsial infection as shown in Figure 1. He had developed dry gangrene of all five toes of the left foot and the second toe of the right foot by the second day of ICU admission as shown in Figure 2. He was hemodynamically stable with noradrenaline and all his peripheral pulses were palpable. There were few scattered coarse crepitations but his saturation was maintained with ventilator support. Abdominal examination revealed a two finger breath hepatomegaly with no other organomegaly, mild free fluid and. Pupils were equal and reactive to light and fundoscopy was normal with no evidence of any focal neurological signs.

We had few differential diagnoses as to whether it was leptospirosis, Hanta viral infection or typhus but with the rash it was more supportive for typhus. Hematological investigations revealed thrombocytopenia and anemia and a microangioapathic hemolytic anemia was confirmed via serial blood pictures. Biochemical investigations revealed an acute kidney injury with a mild hepatitis. The trend in the blood investigations are depicted in the Table 1 below. Leptospira antibodies were negative. Scrub typhus antibodies were negative but the timing had been too early for the detection of antibodies and the facilities for

Indirect Fluorescent Antibody (IFA) levels was not available. HIV, VDRL, HepBsAg, and Hepatitis C antibodies were negative. 2D echo excluded any possibility of infective endocarditis, myxomas and it was normal with a normal ejection fraction. Blood and urine cultures did not reveal any growth. Non Contrast Computed Tomography of the brain was normal. CSF analysis excluded meningococcal sepsis. Vasculitis needed to be excluded since there was a renal and pulmonary involvement at the latter part of the illness thus, ANA, cryoglobulin levels, cANCA, pANCA were negative. ADAMTS 13 assay could not be done due to lack of facilities.

Figure 1 D2 of ICU admission.

Figure 2 D19 during the ward stay after ICU care.

Table 1 Diagnostic focus and assessment

Day of illness (from D7)	D7 (at local hospital)	D9 (at local hospital)	D10 (MICU)	D14 (MICU)	D18 (MICU to ward)
WBC x 10^9	3.5	5.9	12	18	11
Hb g/dl	12.9	11.9	10.4	6.9	8.2
Plt x 10^9	74	26	33	68	116
S.Creatinine µmol/L	86	290	336	206	87
Na/Kmmol/l	138/4.6	136/5.2	137/4.5	147/3.9	150/4.8
BU mg/dl	6	32		18	11
S bilirubin µmol/L	18		111	20	21
D.Bilirubin µmol/L			101	20	21
ALT U/l	41		58	62	53
AST U/l	56		114	119	96
CRP	178		128	50	13
Procalcitonin			3.5	1	0.08

Our working diagnosis was rickettsioses complicated with vasculitis and thrombotic microangiopathy. He was already treated with doxycycline followed by ceftriaxone and showed a marked improvement mainly after starting intravenous chloramphenicol. Intravenous methyl prednisolone was given for three days as well. His acute kidney injury with reduced urine output and rising creatinine

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improved after one episode of sustained low efficiency dialysis (SLED). On the fifth day his saturation dropped and was found to have blood stained secretions and developed fits while he was off paralysis. With the picture of microangiopathic hemolytic anemia, seizures, acute kidney injury, thrombotic thrombocytopenic purpura was clinically diagnosed. He was offered therapeutic plasma exchange (TPE).It was done only twice every other day. There was a significant rise in the platelets and resolution of the alveolar hemorrhages after the second cycle as depicted in the chest X ray (Figure 3 & 4). There was no further evidence of microangiopathic hemolytic anemia in the repeat blood pictures. He was gradually weaned off from inotropic and ventilator support and extubated on day eight. All his clinical parameters had improved and the only residual effect was his dry gangrenous toes which was not progressive with a clear demarcation.

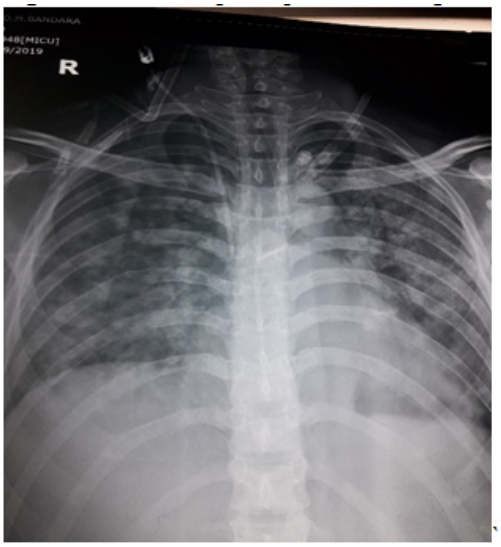

Figure 3 Before therapeutic plasma exchange.

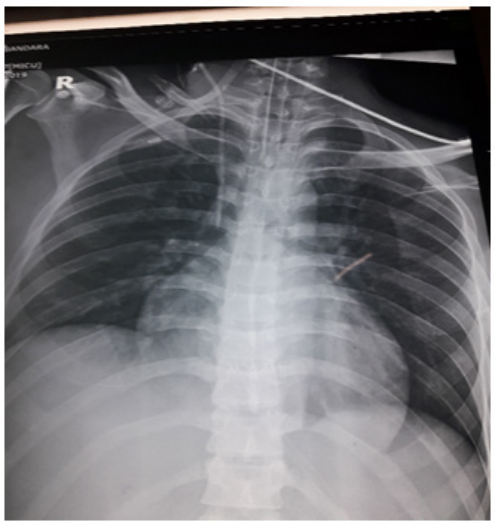

Figure 4 After therapeutic plasma exchange.

He was then transferred to the surgical ward in view of attending to his dry gangrene toes. Initially, he was only observed with no intervention. There was no further progression and about one week later his toes were amputated after getting his informed written consent. The rash had started to desquamate. He had no other complications (Chart).

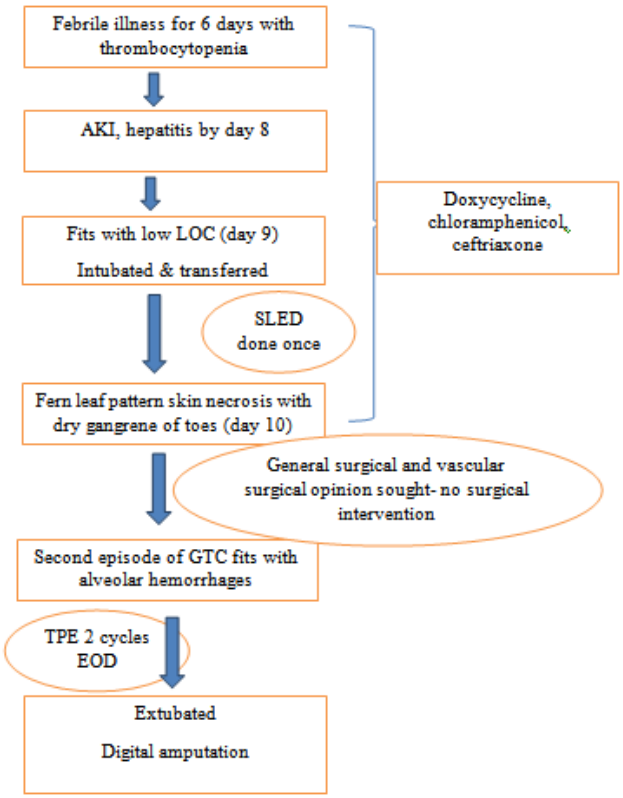

Chart Timeline.

Discussion

Rickettsial infection in Sri Lanka dates back to 1930's and even in 1950's it was a differential diagnosis for clinicians where they suspected typhus in cases of pyrexia of unknown origin but documentation had been only in 1994.[6] Many cases have been reported from the Central Province and also from Mawanella which belongs to the Sabaragamuwa Province. Our patient of interest too is from this area. Geographical distribution of rickettsioses in Sri Lanka is variable.[7] Weil Felix test is considered a non-specific and an obsolete test currently. Indirect Fluorescent Antibody (IFA) assay is considered as a better diagnostic modality but it is time consuming, not freely available (only available at reference centres), expensive and require trained experts for interpretation and carrying out the diagnostic procedures.[8] This is a drawback and reports from certain private laboratories are unreliable which was a similar scenario in our patient. ELISA too can be used as a diagnostic test. Thus clinical suspicion, awareness and experience is a crucial point in managing rickettsioses in developing countries with limited resources like Sri Lanka.

Usual clinical features include high intermittent fever spikes, headache, arthralgia, myalgia regional or generalized lymphadenopathy, hepatomegaly, splenomegaly, presence of an eschar or a maculopapular rash. Complications such as deafness, tinnitus, hepatitis, myocarditis, encephalitis, pneumonitis, acute kidney injury, vasculitic type skin rashes with necrosis (fern leaf pattern in severe cases), haemophagocytic lymphohistiocytosis, digital or limb gangrene and thrombotic thrombocytopenic purpura can occur.[9] Our patient too had multi organ dysfunction which included acute kidney injury, hepatitis, pneumonitis and most of all dry gangrene and thrombotic thrombocytopenic purpura.

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Gangrene is an uncommon complication. It is due to vasculitis, leading to skin rash, microvascular leakage and tissue hypoperfusion.[10] In our patient, the fern leaf pattern was evident which was followed by digital gangrene that extended upto the metatarsophalangeal joints of all digits of the left foot and the second digit of the right foot. There was no administration of unfractionated heparin at any time due to persistent thrombocytopenia so heparin induced thrombocytopenia was not the cause for it. Presence of the pentad of microangiopathic hemolytic anemia, thrombocytopenia, neurologic abnormalities, renal failure, and fever he fulfilled the criteriae for thrombotic thrombocytopenic purpura.[11] However we did not have facilities to perform ADAMTS 13 levels.

Doxycycline is the drug of choice for rickettsioses. Chloramphenicol, a less effective drug is another option for those who are allergic to doxycycline or pregnant.Clarithromycin can be used for milder disease.[12] Other complications such as respiratory failure requires intubation and mechanical ventilation and sustained acute kidney injury requires hemodialysis. There is no evidence that glucocorticoids improve outcome.

Early recognition and prompt treatment with doxycycline is the major determinant of all case mortality and morbidity of rickettsioses. Also, one should be vigilant about the rare complications of rickettsioses which are remediable if approached and addressed at the right moment.

Informed consent

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

Declarations

Ethical declarations

Ethics approval and consent to participate Not applicable.

Availability of data and materials

Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study. All data contained within the article.

Consent for publication

Informed written consent for the publication of details and pictures was obtained from the patient. Consent form can be made available to the editor on request.

Authors' contributions

JMHDJ and WKSK were involved in managing the patient and gathering of data. Literature review and writing of the initial manuscript was done by JMHDJ. WKSK finalized the manuscript and gave expert opinion in management issues. All authors read and approved the final manuscript.

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Not applicable.

Conflicts of interest

The authors declare that there are no conflicts of interest.

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