



An Outbreak of Typhus Fever from Western India

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Abstract

A sudden increase in febrile illness occurred in Western India Shindewadi, Shirur 40 kms from Pune, Maharashtra, August 2016. Fever was the most common presenting symptom and 2 children died at the start of the outbreak. A team was sent from B. J. Govt. Medical College & Sassoon General Hospital, Pune to investigate the outbreak. Blood samples were collected from 25 patients with febrile illness and Controls from the same area. All the samples were tested for a battery of tests for Fever of Unknown Origin (FUO). All affected patients were children in the age group ranging from 2-14 years. Clinically no other symptoms and signs other than fever were observed. Out of 25 samples, 7 (28%) gave evidence of Rickettsial disease by the Weil Felix test. Due to high Weil Felix positivity suggestive of Typhus fever samples were retested for Typhus infection by Rickettsia IgM ELISA kit. 21 (84%) samples were positive for Typhus group. All the patients were treated with Doxycycline. Rickettsial infections seem to be re-emerging in India, so a high index of suspicion must be maintained and tests for Rickettsial diseases should be included in the battery of test for Fever of Unknown origin.

Keywords: FUO Outbreak; Weil felix test; Typhus fever.

Introduction

In India fever of Unknown origin (FUO) is caused by many etiological agents. Rickettsial illnesses have been infrequently reported and majority of them have been due to Rickettsial fever (Scrub typhus) from different parts of India [1,2]. Rickettsial infections are caused by obligate intracellular bacteria of the Rickettsiae family. They are transmitted to humans by arthropods like ticks, fleas, mites, and lice [3]. Rickettsia is classified into four groups namely spotted fever group (SFG), Typhus group, Scrub typhus group and miscellaneous.

Rickettsial infections are spread throughout the world and are re-emerging in the Indian subcontinent, especially among children. Rickettsial infections (fever) have been under reported from India over the last decade. Rickettsial infections were considered to be most neglected re-emerging disease and thus the skills in diagnosis and management is of utmost important and a high index of suspicion should be considered. With early/timely diagnosis treatment of Rickettsial infections is easy, inexpensive and mostly successful [4]. However, these diseases often remain undiagnosed and the lack of treatment leads to fatality rates as high as 30-35% [4]. Multiple factors contribute to the gross under-diagnosis of Rickettsial infections these include the relatively non-specific disease presentation, low index of suspicion, and lack of awareness about its re-emergence [5,6]. The challenge in Rickettsial disease is difficult diagnosis in the early course of disease when the antibiotic therapy is most effective [7].

We report here an outbreak of Typhus fever from Western India from a small rural community Shindewadi, Shirur, 40 kms from Pune in August 2016.

Material and Methods

Blood samples were collected from 25 patients with febrile illness and 16 controls from the same area with no illness. Samples were tested for battery of test for Fever of Unknown origin (FUO) (Table 1).

Test	Manufacturer
Tube Widal test	BEACON diagnostics Pvt. Ltd., Navsari
NS1 antigen ELISA	PAN Bio Standard Diagnostics, Republic of Korea
Dengue IgM ELISA	In-house kit manufactured by NIV, Pune
Chickungunya IgM ELISA	In-house kit manufactured by NIV, Pune
Leptospira IgM ELISA	PAN Bio Standard Diagnostics, Republic of Korea
Rapid Malaria antigen test	OSCAR Medicare Pvt. Ltd., New Delhi
Weil Felix test	Febrile Antigen kit, Omega Diagnostics, UK

Table 1: Test and Manufactures.

All the tests were performed as per manufacturer's instructions. Weil-Felix test results that had titers of 1:80 or more were considered to be highly suggestive of Rickettsial infection [8]. All the samples were retested for Typhus infection by Rickettsia typhi IgM ELISA kit (Fuller Laboratories, USA) and Rickettsia typhi IgG ELISA kit (Fuller Laboratories, USA)

Results

All affected patients (25) were children in the age group ranging from 2-14 years. Clinically no other symptoms and signs other than fever were observed. No rash was seen in any patient. All other test for fever of Unknown origin were negative and out of 25 cases, 7 (28%) gave evidence of Rickettsial disease by the Weil Felix test (Table 2).

Test Done	Positive No (%)
Tube Widal test	0 (0%)
Dengue IgM ELISA	0 (0%)
Chickungunya IgM ELISA	0 (0%)
Leptospira IgM ELISA	0 (0%)
Rapid Malaria antigen test	0 (0%)
Influenza	2 (8%)
Weil Felix test	7 (28%)

Table 2: Result of samples tested (N=25).

Weil Felix tests results were suggestive of Typhus group Rickettsial infection (Table 3).

Patient No.	OX 19	OX 2	OX K
1	Positive (1:160)	Positive (1:160)	Negative
2	Positive (1:80)	Negative	Negative
3	Positive (1:160)	Negative	Negative
4	Positive (1:80)	Negative	Negative
5	Positive	Negative	Negative
6	Negative	Positive (1:160)	Negative
7	Positive (1:160)	Positive (1:160)	Negative

Table 3: Results of the Weil Felix test (N=7).

Due to high Weil Felix positivity suggestive of Typhus fever samples were retested for Typhus infection by Rickettsia typhi IgM ELISA kit. 19 (76%) of samples from febrile children were positive for IgM ELISA and 7 (28%) of febrile children's were IgG ELISA positive. The IgG was positive in control group 8(50%) by Rickettsia typhi IgG ELISA kit. None of the control group showed positivity with Rickettsia typhi IgM by ELISA.

Discussion

Rickettsial diseases are re-emerging and having serious impact on public health as they are misdiagnosed/underdiagnosed and often neglected [9,10-14]. Reports of Rickettsial infections are increasingly being made from countries in various world and reported from many parts of the world and India [9,10-14]. The National Centre for Disease Control (NCDC) has played important role in providing serological evidence of Rickettsial diseases in India in various States like Jammu & Kashmir, Himachal Pradesh, Uttarakhand, Haryana, Rajasthan, Assam, West Bengal, Maharashtra, Tamil Nadu, Kerala, Sikkim, and Manipur in the last decade [4,8,15,16-19]. The reported cases seem to be underrated as there is no single confirmatory test available for the diagnosis of Rickettsial infections.

Rickettsial diseases have been reported from the various parts of India showing a trend of re-emergence. The analysis of published Rickettsial outbreaks in the last era indicates continued occurrence, predominantly scrub and tick typhus, in several parts of the India [12]. A study on tick borne Rickettsiosis in Pune district of Western India

revealed that Indian tick typhus exists as zoonosis [20]. A serological survey conducted by NCDC, Delhi 2012 in patients with suspected FUO identified 8.2% Rickettsial disease by Weil Felix tests with 48.2% cases were Scrub Typhus, 27.5% Spotted fever followed by 6.8% Typhus infection [21].

Majority of Rickettsial outbreaks reported from India have been due to Scrub Typhus group [16,9] This is the first time from Western India that we are reporting Typhus group outbreak of Rickettsial infection. This outbreak seems to be Typhus as IgM ELISA was positive in patients and was having endemic focus for Typhus fever group in this area as shown by IgG ELISA which was positive in control as well as febrile group which shows that Typhus fever infections have endemic focus in this area. Though, further investigations are needed for the isolation of rickettsia from vectors to determine the exact origin and Rickettsia strain prevalent in this part of Western India. 7 blood samples positive by both Rickettsia typhi IgM ELISA kit and Weil Felix test were sent for confirmation by PCR Amplification to AIIMS, Delhi but none of the samples were positive this might be because all the patients were on broad spectrum antibiotics and also the patients were referred to our hospital after 7 days of fever. Micro IFA is a gold standard test for diagnosis of Rickettsial infections but was not available with us to do a confirmatory diagnosis of Typhus fever.

Rickettsial infections are difficult to diagnose and is crucial increase alertness among doctors in Endemic areas to keep a high index of suspicion for diagnosing Rickettsial infections, as these infections are often the last to be suspected [4]. Confirmation of suspected cases by appropriate laboratory tests is clue for documenting the infection. Majority of the outbreaks studied were confirmed by the Weil-Felix test. The present Outbreak was confirmed by both Weil Felix test and Rickettsia typhi IgM ELISA test. Evaluations done by Prakash, et al. (2006) [22] showed that the Weil-Felix test had a Specificity of over 98 % and a Sensitivity of about 43%. Though this test is a historical confirmatory test, done to confirm the occurrence of the infection two weeks after the beginning of the disease rather than to diagnose it in its early stages, it has documented the presence of the disease in several areas [9,23].

The biggest challenge in Rickettsial infections is that difficulty in diagnosis of these infections in there early phase when the antimicrobial treatment is most effective thus Rickettsial infections should be kept in mind while testing and treating patients with FUO [24,25] Doxycycline is the drug of choice along with other supportive measures and it can be used safely even in children below 8 years of age [11,5] Duration of therapy should be at least 3 days after a defervescence or minimum 5-7 days. All the patients in the present study responded well to Doxycycline treatment and no mortality was observed after.

Conclusion

Thus here we are reporting Typhus fever outbreak first time from Western India and Typhus fever infections seems to be endemic in this area. Rickettsial infections seems to be re-emerging in India specially in children's, so a high index of suspicion must be maintained and tests for Rickettsial diseases should be included in a battery of test for FUO so that early treatment can be started to avoid severe disease and fatal outcome.

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