

Clinico-pathological profile of Rickettsial Fever in a rural area of western Maharashtra, India.

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Abstract:

Rickettsial fever is a common ailment in many parts of India with high mortality and morbidity. It can present with a myriad of symptoms like fever, headache, rash, meningoencephalitis, congestive cardiac failure and shock. It can closely mimic multiple illnesses like dengue, meningococcaemia, enteric fever, leptospirosis. Clinical and epidemiological features supported by Weil-Felix test can help in the diagnosis, especially when other serodiagnostic facilities are not available. Fifty cases of Rickettsial fever presented to a tertiary care medical college hospital situated in a rural area of western Maharashtra (from August 2011 to February 2012) is presented with special references to CNS affection. This is probably the only study in which CSF study was done in all 50 patients.

Key words - Rickettsial fever, Weil –Felix test.

Introduction

Rickettsial Fever (RF) is an acute febrile, zoonotic disease spread by bite of ticks or mites. It is now well documented that Rickettsial disease is prevalent all over India and reemerging in various parts of the country [1-8]. The presences of Rickettsial diseases in India have been documented in Jammu & Kashmir, Himachal Pradesh, Uttaranchal, Rajasthan, Assam, West Bengal, Maharashtra, Kerala and Tamil Nadu[5,6,8].

The hallmark of Rickettsial infection is microvasculitis causing microinfarcts in various organs. Usually the patients present with fever, headache and rash (clinical triad). Rash occurs more commonly in children than in adults. Initially, discrete, pale, rose-red blanching macules or maculopapules appear, characteristically on the extremities, including the ankles, wrists, or lower legs. The rash then spreads rapidly to involve the entire body, including the soles and palms. After several days, the rash becomes more petechial or hemorrhagic, sometimes with palpable purpura. In severe disease, the petechiae may enlarge into ecchymoses, which can become necrotic. Severe vascular obstruction secondary to Rickettsial vasculitis and thrombosis is infrequent but

can result in gangrene of the digits, earlobes, scrotum, nose, or an entire limb.

Apart from this, calf pain, oedema, gastro-intestinal symptoms, hepatosplenomegaly, anemia, painless eschar and lymphadenopathy are other manifestations. Complications include meningoencephalitis, acute respiratory distress syndrome, pneumonia, myocarditis, renal failure and vascular collapse.

Rickettsial diseases may pose a serious public health problem if misdiagnosed or not diagnosed. Diagnosis and surveillance of this disease can be challenging, particularly in the absence of advanced laboratory techniques or expensive tests. Microimmunofluorescence, immunoperoxidase assay, latex agglutination, indirect hemagglutination, enzyme-linked immunosorbent assay, dot blot immunoassay (including dipstick test) and Weil-Felix test are the various serological methods available for diagnosis of rickettsial diseases. Tissue or blood can also be evaluated for *R. rickettsii* nucleic acids by polymerase chain reaction (PCR). Immuno-fluorescence antibody (IFA) assay is the gold standard technique and is used as a reference technique in most laboratories.

Weil Felix (WF) test is based on the detection of antibodies to various proteus species which contains antigens with cross-reacting epitopes to antigens from members of the genus Rickettsia. Proteus vulgaris antigen ox 2 cross reacts with spotted fever group, ox 19 with typhus group, RMSF(Rocky mount spotted fever), while ox K reacts with scrub typhus. **Even though WF**

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agglutination test is not very sensitive, but when positive, it is a specific test [9]. Although the sensitivity of WF test has been claimed to be less, there are several reports which suggest good correlation of this test with other standard tests used. Amano et. al. tested sera from 17 patients of Rickettsial disease in the acute and convalescent phases by indirect immuno-peroxidase test, WF test, Enzyme Linked Immuno Sorbent assay (ELISA) and immuno-blotting and compared antibody titres between acute and convalescent phase sera. A parallelism of increment was noted between the titres in the Weil Felix test and titres of immunoglobulin M (IgM) in ELISA. He also observed that of the sera which were positive to Rickettsia by indirect immuno-peroxidase test approximately 80% of the same sera were WF test positive [14,15].

Aims

The present prospective study was carried out to chart the clinical and hematological profile of patients suffering from Rickettsial fever admitted to hospital.

Material and methods:

- 1. **Period of study:** Seven months
- 2. **Sample size:** Fifty patients
- 3. **Inclusion criteria :**

All patients bellow age group of twelve years who were clinically suspected to be suffering from Rickettsial Fever admitted into our hospital, during the period of August 2011 to February 2012 were included in this study. The suspicion of Rickettsial fever was based on history of fever, non-confluent maculopapular or purpuric rash involving palms and soles [fig.1].



Fig-1 : rash involving palm and soles

4. Exclusion criteria :

- a) Patients with confirmatory diagnosis of other disease.
- b) Age more than 12 years.

On admission, a complete physical and routine laboratory investigations such as complete blood count, Liver function tests, Renal function Tests, Weil Felix test, Widal

test, Immunochromatography Dengue & Immunochromatography Malaria and plain X-ray chest were carried out in all patients. CSF was studied for routine microscopy and biochemistry. Meningococcal smear and culture was done in all patients. (since meningococemia closely resembles Rickettsial fever).

All patients were treated with Doxycycline in the dose of 5mg/kg/day once daily for 7 to 10 days. Intravenous Chloramphenicol (75 to 100 mg/kg/day) was added in cases associated with CNS symptoms or abnormal CSF. Blood transfusion was given if hemoglobin was less than 5 g/dl

Results

In present study, 50 patients satisfied the inclusion criteria. Ages ranged from 6 months to 12 years with maximum incidence occurring in around the 5 year age group, with slight male predominance (M:F = 1.2:1). Purpura fulminance was seen in one patient [fig.2]. Lymphadenopathy was absent in all patients.



Fig-2 : Purpura fulminance.

Most of the patients resided in an area of 40 km radius from the hospital. **All patients were from rural area and were living in close proximiy of domestic animals.** All the patients were from low socioeconomic strata. No death was reported in our study.

Table: 1. Clinical features

Sr. no.	Clinical features	No. of cases	Percentage %
1	Fever with rash	50	100%
2	Purpuric rash	6	12%
3	Edema	15	30%
4	Convulsions	18	36%
5	Altered sensorium	6	12%
6	Pain in legs	5	10%
7	Hepatosplenomegaly	33	66%
8	Conjunctivitis	6	12%
9	Upper GI bleeding	6	12%
10	Peripheral gangrene	2	4%
11	Pneumonia	2	4%

Table 2. Haemogram

Test	Value	No	%
Haemoglobin	5.2- 12.5gms. (Mean 9.2 g)	-	-
Leucopenia	<5000	3 patients	6%
Leucocytosis	>10000	29 patients	58%
Thrombocytopenia	<1.5 lakhs	15 patients	30%
Thrombocytosis	> 4.5 lakhs	5 patients	10%

More than half the patients had leucocytosis and a third also had thrombocytopenia.

Table 3. CSF analysis

CSF Features	Nos	%
Neutrophilic predominance	9	40%
Lymphocytic predomance	13	60%
CSF sugar low	10	20%
CSF protein high	14	70%

CSF exqminations carried out is 50 patiats of which 22 were abnormal (44%)

Meningococci were not detected either on gram staining or culture in any of me CSF samples.

Table 4 Weil - Felix test: Results

S.No	OX 19 titre	OX 2 titre	OX K titre	No.of patients
1	1 : 320	1 : 320	-	18
2	1 : 320	1 : 160	-	12
3	1 : 160	1 : 320	-	12
4	1 : 160	1 : 80	-	08
				50 total

Both OX 19 and OX 2 are agglutinated in spotted fever. OX K agglutinated in patients with scrub typhus.

Discussion

Rickettsial disease is an acute infectious disease caused by Rickettsial organism, which is transmitted to humans by ticks, mites or lice[fig-3]. In our study the age of presentation of the disease ranged from 1 month to 12 years with mean age of 5 years. There was no significant sex difference. This is similar in to Colomba et. al. who showed median age of presentation as 6 years with male preponderance (M:F-2.6:1). Majority of the patients presented with fever and rash (100%). A characteristic non-confluent maculopapular rash involving palms and soles was seen in 100%, which was almost similar to the finding of Colomba et. al. Altered sensorium was seen in 12% which was half in comparison to S K Mahajan et. al. (24%). Seizures were seen in 36% in comparison to S K Mahajan et. al. (19%). Hepatosplenomegaly was seen in 66% which was far more in comparison to S K Mahajan et. al. (43%). Conjunctivitis 12%, Peripheral gangrene 4%, and pneumonia 4% were also seen in our study.

Table 5. Comparison of symptoms and signs with others studies [1, 8, and 12].

Symptoms and signs	Present study	Mahajan et al	Colomba et al	Kulkarni A et al
Fever	100 %	100%	100%	100%
Rash	100%	100%	94%	100%
Seizure	36%	19%	-	42%
Altered sensorium	12%	24%	-	71%
Hepatosplenomegaly	66%	43%	-	56%
Conjunctivitis	12%	-	-	-
Gangrene	4%	-	-	51%
Upper GI bleeding	12%	-	-	7%



Fig- 3 : Dog tick

From table 4 it is clear that the if **criteria of single titer of more than 1:320 is considered diagnostic for infection, WF test was positive in 42 out of 50 cases (84%)**[13]. According to WF titres, the most probable Rickettsial disease would be tick borne-spotted fever or Indian tick typhus. Since no louse infestations (scalp and body infestation, lymphadenopathy) was seen in any of the patients and most of them were from low socioeconomic status from rural area and were living near cattle house; probability of tick infestation is very likely. Other investigations like PCR should be done for precise etiological diagnosis of Rickettsial organisms. In our study, CSF examination was done in all patients. There were 28 patients with normal CSF features but 22 patients had abnormal finding (44.44%), 9 patients (40%) showed neutrophilic predominance and 13 patients (60%) showed Lymphocytic predominance. **This is suggestive of a strong association of CNS involvement in Rickettsial fever although signs and symptoms of CNS involvement were absent.** Out of 18 patients who had seizures, 14 patients had abnormal CSF features and rest of them are more likely to be have been suffering from febrile seizures, as these cases belonged to age group of 9 months to 4 years. In our study conducted in hospital setup, Weil-Felix test was positive in 84% cases. The titers varying from 160 to 320.

Conclusion

- 1. What this study demonstrates:** Rickettsial organisms do invade the CNS and CSF abnormalities may be seen in significant number of patients.
- The shortcomings of the study are that only Weil Felix test was done. Other more specific tests may have yielded more precise results. Rashes over the palm and sole can also be present in other diseases like meningococemia and enteroviral diseases and these are difficult to exclude in the absence of facilities for viral isolation and serology.

- The availability and the cost of standard serological methods for Rickettsia like PCR, ELISA are major problems in India. The diagnosis should be largely based on high index of suspicion and careful clinical, laboratory and epidemiological evaluation supported by cost effective tests like Weil-Felix test. Weil-Felix test should be properly interpreted and clinically correlated. The relatively poor sensitivity of the WF test is well known but a good correlation between the results of the WF test and detection of IgM antibodies by an indirect immunofluorescence assay (IFA) is often observed.[16]
- It is suggested that the CSF abnormalities are present in a majority of cases of Rickettsial fever.
- Rickettsial fever can be present with conjunctivitis, generalized oedema, meningoencephalitis and purpura fulminance.
- Empirical treatment with doxycycline, chloramphenicol, should be considered to reduce the high mortality and morbidity observed in this disease.
- In our study no mortality was seen most likely due to early diagnosis and prompt treatment as detailed above.
- Rickettsial fever is prevalent in a rural area of western Maharashtra.

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