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A clinical study of rickettsial disease and its manifestations.

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Abstract

The present retrospective study was conducted to identify the clinical features ,complications and outcome of rickettsial infections in children. Thirty children hospitalized in a period of 18 months with fever of unknown origin and those presented with two or more clinical features suggestive of rickettsial infection were included. These patients were studied for clinical manifestations, response to therapy and complications. Diagnosis of rickettsial disease was made based on classical clinical features and weil-felix test. Out of 30 patients with possible rickettsioses, scrub typhus was diagnosed in 14 (46.7%), spotted fever in 8 (26.7%), typhus in 2 (6.6%) and mixed features in 6 (20%). School going children were commonly affected. Rashes were present in 25 cases (83.3%). Other clinical features include vomiting in 11 cases (36.7%), pain abdomen in 8 (26.7%), diarrhoea in 3 (10%), constipation and jaundice in one case each (3.3%). Examination revealed hepatomegaly in 14 cases(46.7%), associated splenomegaly in 7 (23.3%), conjunctival congestion in 10 (33.3%), pedal edema in 7 (23.3%), lymphadenopathy in 1 case (3.3%). All patients recovered with doxycycline therapy.

Keywords: Rickettsial disease, fever of unkonwn origin, Weil-Felix test.

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Introduction

Rickettsial infections are unique in various aspects. They occur in many countries across the world and are reported from almost all the parts of India. The mortality due to rickettsial infection is more than the mortality caused due to all the wars combined together [1]. As no single laboratory finding is specific for early diagnosis, treatment needs to be started empirically on clinical and epidemiological suspicion. In view of low index of suspicion, nonspecific signs and symptoms, and absence of widely available sensitive and specific diagnostic test, these infections are extremely difficult to diagnose but treatment is easy, affordable and often successful with dramatic response to antimicrobials [2]. Physicians, including pediatricians, usually do not include rickettsial infection in their differential diagnosis [3] and hence antimicrobials effective for Rickettsial disease are usually not included in empirical therapy of nonspecific febrile illnesses.

The incidence of different rickettsial infections depends on the presence of specific vectors and hosts. The transmission of Scrub typhus is associated with trombiculid mites and the hosts for scrub typhus are rodents. Spotted fever group rickettsiae are transmitted by hard ticks, mites, or fleas, and the hosts are rodents, dogs, and wild animals [4,5]. Although rickettsial infections such as scrub typhus and spotted fevers are more common in rural areas, urbanization per se has not contributed to the decline of these infections [5].

In clinical practice as well as in epidemiological surveys, the main difficulty in diagnosis and management of rickettsial infections is the lack of facilities for definitive diagnosis. The most commonly available Weil-Felix test, is now considered obsolete, and better diagnostic techniques, such as indirect fluorescent antibody (IFA) assays, are available only at reference centers. The clinical diagnosis and reporting of rickettsial infections are mainly based on clinical features, such as the presence of eschars or characteristic rashes. Although clinical manifestations of rickettsial infections are well documented, recent studies in Asian countries have reported complications such as gastrointestinal manifestations, tinnitus, and hepatitis syndromes [6]. Awareness about different clinical presentations of these infections may assist in early diagnosis, especially in areas where no diagnostic facilities are available. The objective of this study was to identify clinical features in children with suspected rickettsial infections presenting to a tertiary hospital in Bangalore.

Material and Methods

We conducted a retrospective review of children admitted at our center KIMS, Bangalore between January 2013 and June 2014. Children aged <18 years; hospitalized with fever of unknown origin and presented with one or more of the following clinical features viz; rash, edema, hepatospenomegaly, lymphadenopathy, eschar. History of tick bite or tick exposure were noted. Children with known cause of fever at the time of admission and patients treated on an outpatient basis were excluded. The case definition included patients with high intermittent fever and having at least five out of the following eight clinical features namely; headache, myalgia, regional lymphadenopathy, generalized lymphadenopathy, hepatomegaly, splenomegaly, presence of an eschar, or presence of a maculopapular rash. The clinical course of the illness and complications of infection were recorded.

Results

All the 30 patients met the inclusion criteria (13males and 17 females). All patients presented as sporadic cases and were living on an average of 20 km (range 2-60 km) from the hospital. 30 cases fell into the categories of confirmed, presumptive, or exposed cases of acute rickettsial infections. Scrub typhus was diagnosed in 14 (46.7%), spotted fever group in 8 (26.7%), typhus group in 2 (6.7%) and remaining 6 (20%) were showing mixed features.

Weil felix was positive in 18 (60%) cases and the remaining were clinical diagnoses. They presented with fever for a period of 3days to 20 days (mean of 8.3 days). The age group of children admitted was between 1.1yrs and 15yrs (mean of 7.2yrs) with a female preponderance (56.7%).

Table 1. *Distribution of type of rash in cases.*

Distribution of type of rash	Number of cases (out of 30 cases)
Maculopapular	13(43.3%)
Erythematous	8(26.7%)
Erythematous maculopapular	5(16.7%)
Petechial	4(13.3%)
Purpuric	4(13.3%)
Eschar	2(6.7%)

The clinical features involved many organ systems. Vomiting was present in 11 cases (36.7%), pain abdomen in 8 (26.7%), diarrhoea in 3 (10%), constipation in 1 case (3.3%). Jaundice was present in 1 case (3.3%), hepatomegaly in 14 (46.7%), associated splenomegaly in 7 (23.3%), conjuctival congestion in 10 (33.3%), pedal edema in 7 (23.3%), lymphadenopathy in 1 case (3.3%) .

All the patients presented with complaint of fever (100%), but out of them associated chills were presented only in 12 cases (40%), headache only in 5 cases (16.7%). Rashes were present in 25 case (83.3%), not all cases with presumptive or clinical rickettsial infection presented with rashes. Out of which, rashes first started on face in 12 cases, on lower limbs in 8 cases, on upper limbs in 2 cases and on trunk in 3 cases. Onset of rash was seen from day 1 to day 13 of fever (mean of 3.6 days) . Rash on palms and soles is present in 14 cases (46.7%). Erythematous rash is seen in 8 cases (26.7%), maculopapular rash in 13 cases (43.3%), erythematous maculopapular rash in 5 cases (16.7%), petechial rash in 4 cases (13.3%), purpura in 4 cases (13.3%). Eschar was present in 2cases (6.7%) and associated gangrene or tissue necrosis in one case.The rashes were most prominent when the patients were febrile. There were no hemorrhages associated with the rashes.

Table 2. *Distribution of clinical features.*

Distribution of clinical features	Number of cases
Fever	30
Hepatomegaly	14
Vomiting	11
Conjunctival congestion	10
Pain abdomen	8
Splenomegaly	7
Pedal edema	7
Headache	5
Diarrhoea	3
Constipation	1
Jaundice	1
Lymphadenopathy	1

Various laboratory abnormalities were observed among cases. They were mild anemia with a mean haemoglobin of 10.58g%, thrombocytopenia seen in 7 (23.3%), hypoalbuminemia in 6 (20%), leucocytosis 8 and normal to low leucocyte count in 22cases.

There were other findings such as burning of soles, burning of face, generalised bodyache, altered sensorium, super infections, associated urinary tract infection, hyponatremia , bilateral joint pains , enlarged tonsils , blisters over the ankle and eschar , hyperpigmentation of knuckles.

All our cases responded to doxycycline therapy and there were no sequelae.

Discussion

While rickettsial diseases are reported from various parts of India [7-11], this study shows their clinical manifestation and complications which would facilitate early diagnosis.

However, the reported cases underestimate the burden of rickettsial diseases in India due to the lack of both community based studies and nonavailability of specific laboratory tests [12]. We are reporting a series of cases that were diagnosed during a short period of time .Rickettsial infection in our series is prevalent among all age groups and the youngest child was only 1year 1 month old. Majority of our cases were reported during the months from October to march .Scrub typhus was more common than Spotted fever group and few cases of typhus fever were identified. Kamasaru *et al*. [13] reported higher incidence of ST in Tamil Nadu, whereas SFG was more common in a case series reported by Kulkarni *et al*. [10] from the Western part of India . More recently, a single case of scrub typhus was reported from Mumbai .

Although most of our patients had clinical features suggestive of rickettsial infections that are well documented in the literature, their diagnosis was usually missed at first contact. The lack of awareness of the re-emergence of rickettsial diseases might be the underlying reason [4]. At the time of their presentation to the hospital, many of our patients had received one or more antibiotics at first contact. However, none of these antibiotics were anti-rickettsial agents.

The sharing of antigens between rickettsia and proteus is the basis of Weil-felix , a heterophile antibody test. It demonstrates agglutinins to *Proteus vulgaris* strain OX 19, OX 2 and OX K. Most of the Western workers are not using this test for diagnosis of rickettsial infections. The low sensitivity of the WF test is now well demonstrated 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. This can be used as a screening test, which detects more cases than clinical evaluation alone and when positive, is reasonably specific. In spite of all its drawbacks, Weil-Felix test still serves as a useful and cheap diagnostic tool for laboratory diagnosis of rickettsial disease. Either four fold rise in agglutinin titre in paired sera or single titre of more than 1:320 is considered diagnostic for infection with these agents. The use of this test is accepted in conditions where definitive investigations are not available . Isaac *et al* [14] have demonstrated that the sensitivity of Weil-Felix as 30% at a breakpoint titre of 1:80, but the specificity and positive predictive value were 100%. Hence Weil-Felix test is still not entirely obsolete but has to be interpreted in the correct clinical context [7].

After admitting in the hospital, weil-felix was done in view of suspecting rickettsial infection and were started on doxycycline for 5 days for which they responded well. Some patients with pyrexia of unknown origin with all other investigations being negative including weil-felix were started on empirical treatment with doxycycline for which they responded very well and were graded as clinical rickettsial infection. A few cases with a long duration of pyrexia, with onset of rash after long duration of fever, with missed rickettsial disease went into systemic complications which however responded well after starting with doxycycline as empirical treatment. There was no mortality in the present series.

Conclusion

Weil Felix test can serve as initial but not the only method to diagnose rickettsial diseases, particularly if no rickettsioses have been previously isolated or detected in the area. Therefore, it is possible for most of the microbiology laboratories across the country to start Weil Felix test to assess the burden in their area. Our research shows that rickettsial infections are one of the important causes of FUO and active surveillance of rickettsial diseases is required to know the exact magnitude and distribution of vector and diseases.

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