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Original Research Article

Hyponatremia: a diagnostic marker for the diagnosis of Rickettsial diseases

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ABSTRACT

Background: Rickettsial infections are re-emerging in Indian subcontinent, it is difficult to diagnose among children's in seasonal conditions, an early recognition with clinical and laboratory findings give good response to treatment and avoid unnecessary investigations in limited resources.
Methods: The case sheets of all 60 children's aged <18 years were retrieved and reviewed retrospectively, who are both clinically and serologically confirmed as Rickettsial disease cases were included in this study.
Results: Fever for more than 1week was the most common manifestation, followed by splenomegaly (40%), rash (33%), cough (30%), altered sensorium (16%), and seizures (10%). In laboratory investigation Hyponatremia (56%), elevated liver enzymes without significant rise of bilirubin (28%), hypoalbuminemia (28%), and thrombocytopenia (38%). Patients were treated with Doxycycline, Azithromycin. There was no mortality.
Conclusions: Rickettsial infections are notoriously difficult to diagnose in seasonal condition, untreated cases can have fatality as high as 30-35%, when diagnosed, it is easily treated. Majority of case showed Hyponatremia, may be used as marker in limited diagnostic laboratory facilities.

Keywords: Hyponatremia, Rickettsial diseases

INTRODUCTION

Rickettsial infections is prevalent throughout the world. Rickettsial diseases are now established as re-emerging zoonotic bacterial infections in the Indian subcontinent and are an important but often under-recognized cause of febrile illness among childrens.[1] Rickettsial infections were long considered disease confined to forests and were a rarity in routine practice. Rickettsia is a communicable disease transmitted to man by arthropod vectors (except Q fever).

The organism will not show up on Gram stain, but can be seen through Gimenez or Giemsa stains. They grow readily in yolk sac of the embryonted egg. History-Napoleon's retreat from Moscow was forced by Rickettsial (typhus group) disease breaking out among his troops. There were 25 million deaths in Russia (1917-1922). Lenin is said to have remarked, in reference to louse born typhus disease rampant during Russian revolution, that "either socialism will defeat the louse or the louse will defeat the socialism".[2] In the recent years, outbreak have been reported in the Sub-Himalayan belt, as well as in Maharashtra, Rajasthan, Punjab, and southern states of Tamil Nadu, Kerala, and Karnataka.[3] In Karnataka, although scrub typhus has been reported in the various rural districts, data from the urban surroundings are lacking.

Diagnostic will be a problem because of varied clinical presentation, due to difference in infecting strain.[4] Clinical symptoms overlap with other infectious diseases in seasons with dengue fever, malaria, paratyphoid, and pyrexia of unknown origin (PUO). There is a lack of

proper diagnostic techniques in low-income settings such as India. Immunofluorescence assay (IFA) is a Gold standard, expensive and expert require.[3] Weil Felix is most widely used, but poor sensitivity and specificity.[5]

METHODS

We conducted retrospective review of children admitted between July 2015 and September 2016 at SSIMS and RC, Davangere.

Inclusion criteria

Age <18 years; hospitalized with fever without a source, presence of one or more of the following clinical features: rash, oedema, hepatosplenomegaly, pain abdomen, cervical lymphadenopathy, pain over joints.

Exclusion criteria

The cause of the fever known at the time of admission; and patient treated on an outpatient basis.

Sixty patients qualified for the review, the clinical and laboratory data were collected from the patients' medical records.

Data contains gender, symptoms, signs, lab findings, Rickettsial group.

Investigations

Complete blood count, serum electrolytes, liver function test, weil-felix test was done and titre of 1: 80 or more was considered as positive test, weil-felix slide agglutination test also done to know type of Rickettsial groups, dengue serology were tabulated.

The suspected cases were treated with doxycycline; (dose 5 mg/kg/day for 5-7 days) and response to treatment were recorded. In seriously ill patient's doxycycline was given by Ryle's tube.

The diagnosis of Rickettsial disease was made by the positive weil-felix test, exclusion of other diseases like measles, typhoid, dengue, malaria, pneumonia, nephrotic syndrome, collagen vascular disease and adverse drug reactions done by relevant investigations and prompt response to doxycycline treatment.

RESULTS

In all 60 children's who were diagnosed with Rickettsial disease at SSIMS and RC, Davangere during the period July 2015 to September 2016, there was a 53% female preponderance (32 female versus 28 male). The youngest was 6-month-old while the oldest in the study was 17 years old. The main presenting complaint was fever in all cases 56% for 1 week (n = 34), 38% for 5 days (n = 23), and rest presented after 10 days (n = 3). Along with, rash (1/3rd), cough (1/3rd), gastro-intestinal (vomiting, pain abdomen, abdominal distention) 28% cases, 16% presented with CNS symptoms (altered sensorium), seizures in 10% cases (Table 1). Rarely patients present with one or more complaints like joint pain especially knee, pedal oedema, swelling around eyes or puffiness of face.

Table 1: Clinical symptoms of cases.

Symptoms	No. of patient (n = 60)	Percentage (%)
Fever	60	100
Rash	20	33
Cough	18	30
Vomiting	17	29
Altered sensorium	10	17
Seizures	6	10

Most of the cases suspected as dengue fever, relevant investigation like dengue serology was negative in 30 cases out of 35 cases.

Table 2: Clinical sign noticed in cases.

Signs	No. of patient's (n = 60)	Percentage (%)
Hepatomegaly	34	57
Splenomegaly	24	40
Lymphadenopathy	18	30

Table 3: Laboratory findings in cases

Lab values	No. of patient's	Percentage (%)
Hyponatremia	36/48	75
Hypoalbuminemia	17/34	50
Leucocytosis	25/55	45
Thrombocytopenia	23/55	42

Table 4: Types of Rickettsial group among cases.

Rickettsial group	No. of patient's (n = 60)	Percentage (%)
Typhus group	21	35
Scrub typhus	17	28
Spotted fever group	2	3
Mixed	20	34
Total	**60**	**100**

In serum electrolytes, among 60 cases we noticed hyponatremia was predominant in 34 cases. According to 20th edition of Nelson, Na level <135 mEq/l considered as hyponatremia. Hyponatremia was present both in scrub typhus and typhus group. There was no mortality noted. The poor sensitivity of weil-felix test is now well demonstrated but a good correlation between the results of the weil-felix test and detection of IgM antibodies by

an indirect immunofluorescence assay is often observed. Weil-Felix test can be used as a screening test which detects more cases than misdiagnosed once and when positive, is reasonably specific.[3]

Table 5: Comparison of present study with other studies.

Characteristic	Present study	Thomus R et al[11]	Kalal BS et al[12]
Sample size	n = 60	n = 262	n=62
Duration	1 year 2015-16	5 year 2008-12	2 year 2010-12
Gender	Female (53)	Male (61)	Male (71)
Fever	All	All	All
Rash	33%	54.2%	35.5%
Respiratory symptoms	30%	20.2%	-
GIT symptoms	28%	-	-
CNS symptoms	26%	28%	32.2%
Hepatomegaly	56%	87%	71%
Splenomegaly	40%	50%	37.1%
Lymphadenopathy	30%	21.8%	46.8%
Hyponatremia	60% (Na = <135)	11.5% (Na = <130)	3% (n = 39) (Na = <125)
Elevated liver enzymes	28%	35%	76.2%

DISCUSSION

Rickettsial diseases is a re-emerging infection in India and other parts of South East Asia.[5] Particularly scrub typhus and Indian tick typhus.[6] It was initially reported in endemic form in Karnataka, Vellore, Himachal Pradesh but increasingly cases reported from other parts of India. Most outbreaks are during rainy season and cooler months.[7] In the present study, most of the cases were seen during the months of August to November, such post-monsoon seasonality was reported earlier.[8] Fever is a universal symptom in all patients and other studies.[7] There was no clear localizing symptoms in vast majority. This feature is noted in other case series.[9] The presenting features of this disease include fever, rash, cough, abdominal pain/distention and vomiting. Hepatomegaly, splenomegaly, lymphadenopathy reported in other case series.[10] The commonest complications were altered sensorium, seizures. Hearing loss is reported as a common complication from scrub typhus in Sri Lanka. Hyponatremia (reflecting increased vascularity) is an important laboratory finding and an early finding to differentiate it from other infections, seen in other studies.[3]

Other finding includes leucocytosis, thrombocytopenia, and elevated liver enzymes. The weil-felix test is the widely-used modality even though it is low sensitivity and specificity. However, it is widely available and continues to be the modality of choice in resource limited settings.[10] We treated 10 suspected patient's considering hyponatremia as a marker along with clinical features of Rickettsial disease. They responded well to treatment even though weil-felix test was negative.

What is already know

- Rickettsial diseases are notorious to diagnose.
- High degree of suspicion required in seasonal condition.
- Early treatment better outcome.

What this study adds

- Paediatrician always keep one differential diagnosis of Rickettsial diseases in seasonal condition and fever of unknown source.
- Along with clinical feature, lab findings Hyponatremia as a marker will be helpful to add Doxycycline in the treatment and prevent unnecessary investigations.

Limitation of study was a retrospective review study from a single centre with less sample size. Further studies required to find the true prevalence of Rickettsial diseases with reliable diagnostic method.

CONCLUSION

Rickettsial disease are re-emerging infectious disease, difficult to diagnose in seasonal condition, untreated cases can have fatality as high as 30-35%, when diagnosed, it is easily treated, mortality unusual. Low levels of IgG in general population indicates susceptibility and increased risk of complication.

Diagnosis

Relies on clinical symptoms, delay lead to morbidity because of vascular pathology.

Weil-felix test

Easily available in India, detect antibodies only after 5-7 days of onset of disease, hence play no role for initiation of therapy and early diagnosis. We noticed hyponatremia was present both in scrub typhus and typhus group of Rickettsial disease, in some studies they made some criteria (including hyponatremia) to diagnose only in scrub typhus. In this study majority of case showed hyponatremia, may be used as marker in limited diagnostic laboratory facilities. Awareness of the existence of Rickettsial infection will also prevent excess investigations in patients with fever of unknown sources and lowers the economic burden to families. Further studies are needed to make standard criteria to diagnose Rickettsial diseases in seasonal conditions.

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