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ORIGINAL ARTICLE

Rickettsial Meningoencephalitis : An under diagnosed entity in developing countries

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Abstract:

Rickettsial infections form a diverse group of infections cause by obligate intracellular coccobacilli. Children less than 15 years are known to be the commonest group affected. The disease which is transmitted by vector such as the tick, mite and flea is divided into 3 biogroups – scrub typhus, typhus and the spotted fever groups. We present the profile of a case series of children diagnosed as rickettsial meningoencephalitis, who were referred to our hospital with a provisional diagnosis of either pyogenic meningitis, viral encephalitis or tubercular meningitis. Of the 122 children admitted with rickettsial fever during the study period, 31% had features of meningoencephalitis. The most common age of presentation was 5 years and above. The common clinical manifestations in these children included fever (100%), headache (100%), maculopapular rash (68.4%), seizures (94.7%) and altered sensorium (89.4%). Investigations revealed polymorphonuclear leucocytosis with relative monocytosis, hyponatremia with CSF findings suggestive of elevated counts and raised protein. All children were treated with doxycycline and azithromycin for 7 days with complete recovery. We aim to create more awareness among clinicians with regard to this treatable cause of neuroinfection which if diagnosed and treated early, have a relatively good prognosis.

Keywords: *rickettsia, meningoencephalitis, children*
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Introduction

Rickettsial infections are caused by the microorganisms belong to the family of rickettsiaceae and are obligate intracellular cocco-bacilli [1]. The causative organism was named after Howard Ricketts, who was the first to demonstrate the role of the tick (Dermacentor andersonii) as the vector for the disease in western Montana in the US in 1906 [2]. The illnesses caused can be divided into 3 main biogroups – Spotted fever, typhus and scrub typhus groups [3]. The most frequent presenting symptoms of the illness include fever, headache, rash, and myalgias [4]. Rickettsial fever has been reported to be endemic in the Himalayan belt, Maharashtra and Karnataka in India among the adult population [5]. Pediatric data on the same is limited in developing countries. Recently, the profile of rickettsial fever has been described in children in South India with similar clinical features [6].

However, in spite of the many case series on this disease entity, many clinicians are unaware and are not comfortable making the diagnosis of rickettsial meningoencephalitis and continue to diagnose the same as viral encephalitis, pyogenic meningitis or tubercular meningitis. We report a case series of the varied clinical manifestations rickettsial fever concentrating on meningoencephalitis, a rare complication of the illness with an objective to create more awareness among clinicians.

Material and Methods

Study design

This was a prospective study conducted from September 2010 to December 2011 in the pediatric

intensive care unit (PICU) of Indira Gandhi Institute of Child Health, a tertiary care children's hospital in Bangalore. The population that the hospital caters to belongs to a semi-urban and rural population belonging to the middle and lower socio-economic class. The annual admissions to the children's hospital are around 9500 to 10,000 per year with 2500 to 3000 admissions in the pediatric ICU (PICU) and Step-down ICU.

Study subjects

Children were diagnosed as rickettsial fever on clinical grounds and were considered positive by the Weil-Felix test (titers > 1:160). Meningoencephalitis was diagnosed in the presence of 2 of the following 3 (1) Altered sensorium/consciousness (2) Alteration in behavior or cognition and (3) Seizures, along with CSF analysis suggestive of infection. Each child was investigated with complete blood picture, Serum electrolytes, lumbar puncture for CSF analysis and Weil Felix test. The Weil Felix test antigens Proteus vulgaris OX2, P. vulgaris OX19 and P. mirabilis OXK were obtained. The test was done using standard protocol with doubling dilution of 1:20 to 1:160 for initial screening followed by further dilutions (from 1:20 to 1:1280) to achieve end tire [7]. Elevated OXK titers were suggestive of scrub typhus, elevated OX2 of spotted fever group and OX19 titers were suggestive of the typhus group. All children with rickettsial encephalitis were treated with Doxycycline (5mg/kg/day) for 7 days along with intravenous Azithromycin (10mg/kg/day) for 7 days.

Results

The total number of children admitted with rickettsial fever during the study period was 122 children. Of these, 38 fulfilled the criteria for meningoencephalitis accounting for 31.1% of study subjects.

As shown in Table 1, the most common age of presentation with rickettsial fever was more than 10 years (45%); however, rickettsial meningo-encephalitis was seen more commonly in children aged between 5 to 10 years (57.9%). The gender distribution of the subjects was found to be almost equal with males constituting 56% (n=68) of the total subject population, and 55% (n=21) of children with rickettsial encephalitis. Of the 38 children diagnosed as rickettsial meningo-encephalitis, 12 (31.5%) were referred to our hospital as pyogenic meningitis, 13 (34.2%) as viral encephalitis and 13 (34.2%) as tubercular meningitis to our hospital for further management.

Table 1 also shows the clinical features of children presenting to the hospital with rickettsial fever, with all patients manifesting with fever (100%), 75% with Maculopapular rash and 73% with hepatomegaly. In children with rickettsial meningoencephalitis, 100% presented with fever, 94.7% with convulsions and 89.4% with altered sensorium. In these children the mean Glasgow Coma Score (GCS) was 9.12 (SD 1.62) at admission.

Investigations done in study subjects are shown in Table 1. Leucocytosis and hyponatremia were significant features irrespective of the presence or absence of meningoencephalitis. On the differential counts, polymorph predominance was seen with relative monocytosis. CSF analysis in children with meningoencephalitis demonstrated a poly-morpho-nuclear prominence with elevated protein and near normal glucose.

As shown in Table 2, the Weil-Felix test showed titres between 1:160 to 1:320 in 39.3% children and titres between 1:320 to 1:640 in 37.8% of children. The predominant titres included OX K in 49.2% children followed by OX2 in 47.5% (Table 3). Thus, scrub typhus was the most common type of rickettsial infection in the study group followed by the spotted fever group. The mortality rates in children with rickettsial fever was found to 7.3% (n=9), with ARDS being the commonest cause of death. The mortality in children with rickettsial meningo-encephalitis was 2.6% (n=1) which was a child with associated multiorgan dysfunction. All children with rickettsial meningoencephalitis were treated with Doxycycline (5mg/kg/day) for 7 days. Intravenous azithromycin (10mg/kg/day) for 7 days was added as treatment in children with altered sensorium.

Discussion

The varied manifestations of rickettsial meningoencephalitis in children are demonstrated in our study. Our study shows a predominance of meningoencephalitis in children between 5 to 10 years of age which was consistent with previous studies which report that nearly two-third of all rickettsial fevers occur in children less than 15 years of age [8]. Thus this is an important age group of children who manifest with complications of rickettsial infections. In our study there was an equal

Table 1. Demographic characteristics, clinical features and investigations in children with rickettsial fever

Characteristics	Subjects with rickettsial fever	Subjects with rickettsial meningoencephalitis	Subjects without rickettsial meningoencephalitis
Age [n / (%)]			
< 1 year	3 (2.5%)	0 (0%)	3 (2.5%)
1 to 5 years	30 (24.5%)	6 (15.8%)	24 (28.5%)
5 to 10 years	34 (27.8%)	22 (57.9%)	12 (14.3%)
>10 years	55 (45%)	10 (26.3%)	45 (52.5%)
Total	122 (100%)	38 (100%)	84 (100%)
Clinical features [n / (%)]			
Fever	122 (100%)	38 (100%)	84 (100%)
Maculopapular rash	92 (75.4%)	26 (68.4%)	66 (78.5%)
Eschar	12 (9.8%)	8 (21%)	4 (4.7%)
Headache	89 (72.9%)	38 (100%)	51 (60.7%)
Convulsions	36 (29.5%)	36 (94.7%)	0 (0)
Altered sensorium	34 (27.8%)	34 (89.4%)	0 (0)
Hepatomegaly	89 (72.9%)	32 (84.2%)	57 (67.8%)
Splenomegaly	56 (45.9%)	18 (47.3%)	38 (45.2%)
Lymphadenopathy	48 (39.3%)	16 (42.1%)	32 (38%)
Investigations (Mean ± SD)			
Hemoglobin (g%)	9.6 ± 2.1	9.2 ± 2.2	9.6 ± 2.3
Leucocyte count/cmm	14.360 ± 2300	15,200 ± 1920	14,180 ± 1800
Polymorphs (%)	68 ± 12	72 ± 15	66 ± 14
Lymphocytes (%)	36 ± 15	38 ± 18	34 ± 16
Monocytes (%)	10 ± 3.4	11± 4	10 ± 3.2
Platelet count (lakhs/cmm)	1.8 ± 0.5	1.62 ± 0.54	1.56 ± 0.5
Serum sodium (mEq/L)	128 ± 6.5	126 ± 6.2	128 ± 6.1
CSF Analysis (Mean ± SD)			
Total cells (/cmm)	N/A	89 ± 6	N/A
Polymorphs (%)	N/A	20 ± 18	N/A
Lymphocytes (%)	N/A	82 ± 12	N/A
Protein (mg %)	N/A	79 ± 26	N/A
Glucose (mg %)	N/A	45.6± 14	N/A

gender distribution, although males are known to be affected more commonly with rickettsial infections [9]. Clinical features most commonly seen in our patients included fever, headache, maculopapular rash and hepatosplenomegaly. This has been similarly described in other descriptive studies on rickettsial fever [10]. A rash was seen in 75% of children, which could be due to the evanescent nature of the same [11].

Table 2. Profile of the Weil Felix test in children with rickettsial fever

Titres at time of diagnosis	Children with rickettsial fever [n / (%)]	Children with rickettsial encephalitis [n / (%)]	Children without rickettsial encephalitis [n / (%)]
1:160 to 1:320	48 (39.3%)	12 (31.5%)	36 (42.8%)
1:320 to 1:640	46 (37.8%)	14 (36.8%)	32 (38%)
1:640 to 1:1280	22 (18%)	10 (26.4%)	12 (14.4%)
>1:1280	6 (4.9%)	2 (5.3%)	4 (4.8%)

We report children with rickettsial meningo-encephalitis presenting with fever (100%), headache (100%), convulsions (94.7%) and altered sensorium (89.4%) and with poor GCS, suggestive of intracranial manifestations. Signs of meningo-encephalitis have been described in many studies, while others report meningismus without abnormal CSF findings. Other neurologic findings rarely reported include cortical blindness, central deafness, ataxia, paralysis, and cranial palsies. We however did not encounter any such complications in our patients. It can be seen that nearly one-third of the children were referred as either pyogenic meningitis, one-third as viral encephalitis and one third as tubercular meningitis to our hospital. This thus re-enforces that rickettsial encephalitis does present with similar features as other neuroinfections but more awareness is required to make the correct diagnosis and thus treat them appropriately.

Table 2. Rickettsial antigen positivity.

Titres at time of diagnosis	Children with rickettsial fever [n / (%)]	Children with rickettsial encephalitis [n / (%)]	Children without rickettsial encephalitis [n / (%)]
OX K +	60 (49.2%)	20 (52.6%)	40 (47.6%)
OX 2 +	58 (47.5%)	18 (47.4%)	40 (47.6%)
OX 19 +	4 (3.3%)	0 (0)	4 (4.8%)

Investigations done in these children demonstrated poly-morpho-nuclear leucocytosis, relative monocytosis, and hyponatremia as the predominant markers which favoured a diagnosis of rickettsial disease. The diagnosis of rickettsial fever in our study was made by serological tests [12,13]. Serologic testing for the various species may be expensive and difficult in a resource limited setting. The Weil-Felix test has proven to be a cheaper alternative and can be rapidly performed to substantiate the diagnosis, in spite of its low sensitivity and specificity [14]. In developing countries like India where rickettsial infection is relatively under diagnosed, a cheaper and more widely available option like the Weil Felix test would help as an initial investigation to guide the clinician.

Whole cells of P. vulgaris OX2 has been shown to react strongly with serum from person infected with spotted fever group (SFG) of rickettsiae and hence a marker of the same. OX19 titres are shown to reflect react infection with typhus group of rickettsial infection as well as with Rocky Mountain spotted fever (RMSF) [15]. Also, OXK strain of P. mirabilis agglutinates with serum from scrub typhus patients and hence used to diagnose the same [16]. Studies have shown that rickettsial infections are a common cause of fever of unknown origin in India. Studies conducted in the subcontinent have demonstrated the benefit of the Weil Felix test in diagnosis and treatment of rickettsial infection [17]. Hence using a simple test like the Weil Felix test in a resource limited setting where immunoflourescence, Western blot or PCR based tests are unavailable, would prevent the delay in the diagnosis and treatment of children [18].

A lumbar puncture needs to be performed in children with features of meningoencephalitis to exclude other diagnosis and establish neuroinfection. CSF findings in our study were suggestive of meningoencephalitis with no feature exclusive to rickettsial infections. Rickettsial fever is known to respond dramatically to antimicrobial therapy within 48 hours, and in the absence of such a response, the diagnosis of rickettsial fever needs to be reconsidered [19]. We have treated all our patients with doxycycline for 7 days. In view of decreased oral acceptance in children with an altered sensorium IV azithromycin was added for 7 days in some patients. Doxycycline is known to be the drug of choice even in children, with no complications such as teeth staining or any other noted owing to the short duration of treatment [20]. Supportive treatment for thrombocytopenia, bleeding tendencies and hyponatremia is recommended as in other disease conditions.

Avoidance of contact with mites, fleas and ticks remains an integral part in the prevention of rickettsial infection. The overall mortality rate without specific therapy is approximately 25% with higher mortality seen in older age groups. In the United States, the overall mortality rate currently is 5-7%. Fatalities are mainly caused by delay in diagnosis and treatment. Thus increasing awareness even in developing countries regarding rickettsial fever and its complications would improve the mortality and morbidity of this disease. The relatively good outcome of rickettsial meningoencephalitis in children as shown in our study is promising and further enhances the need for education of primary care pediatricians on this entity in developing countries.

References

1. Walker DH. Rickettsiae and rickettsial infections: the current state of knowledge. Clin Infect Dis. Jul 15 2007;45 Suppl 1:S39-44
2. Ricketts HT. A micro-organism which apparently has a specific relationship to Rocky Mountain spotted fever. JAMA 1909;52: 379 – 380
3. Jensenius M, Fournier P, Raoult D. Rickettsioses and the international traveler. Clin Infect Dis. 2004;34(10):1493-9
4. Helmick CG, Bernard KW, D'Angelo LJ. Rocky Mountain spotted fever: clinical, laboratory, and epidemiological features of 262 cases. J Infect Dis 1984;150:480 – 488
5. Padbidri VS, Gupta NP. Rickettsiosis in India: A review. J Indian Med Assoc 1978; 71: 104-107
6. N. Murali, Swathi Pillai, Thomas Cherian, P. Raghupathy, V. Padmini, Elizabeth Mathai. Rickeetsial infections in South India: How to spot the spotted fever. Indian Pediatrics 2001; 38: 1393-1396
7. Marmion BP, Worswick DA. Coxiella burnetii and other medically important members of the family Rickettsiaceae. In: Collee JG, Marmion BP, Fraser AG, Simmons A, editors. Mackie and McCartney practical medical microbiology. New York: Churchill Livingstone; 1996.
8. Edwards MS, Feigin RD. Rickettsial diseases. In: Feigin RD, Cherry JD, Demmler GJ, Kaplan SL, eds.Textbook of Pediatric Infectious Diseases. 5th ed. WB Saunders Co; 2004:2497-2515/Chapter 195.
9. Rovery C, Raoult D. Meditteranean Spotted Fever. Infect Dis Clin N Am. 2008;22:515-530.
10. Abramson JS, Givner LB. Rocky Mountain spotted fever. Pediatr Infect Dis J. Jun 1999;18(6):539-40
11. Sexton DJ, Corey GR. Rocky Mountain "spotless" and "almost spotless" fever: a wolf in sheep's clothing.Clin Infect Dis. 1992;15(3):439-48
12. Ormsbee RA, Rickettsia. In: Practical Medi-cal Microbiology, 13th edn. Eds. Collee JG, Duguid JP, Fraser AG, Marmion BP. New York, Churchill Livingstone, 1989; pp 742-743.
13. Kovacova E, Kazar J. Rickettsial diseases and their serological diagnosis. Clin Lab 2000; 46: 239-245
14. Bhattacharya D, Mittal V, Bhatia R, Sehgal S. Comparison between indirect fluorescent antibody and Weil-Felix tests for detecting antibodies against rickettsia. J Commun Dis 1991; 23: 144-148.
15. Amano K, Hatakeyama H, Okutta M, Suto T, Mahara F. Serological studies of antigenic similarity between Japanese spotted fever rickettsiae and Weil Felix test antigens. J Clin Microbiol. 1992;30:2441–6
16. Amano K, Suzuki N, Hatakeyama H, Kasahara Y, Fujii S, Fukushi K, et al. The reactivity between rickettsiae and Weil-Felix test antigens against sera of rickettsial disease patients. Acta Virol.1992;36:67–72
17. Dass R, Deka NM, Duwarah SG, Barman H, Hoque R, Mili D, Barthakur D; Characteristics of pediatric scrub typhus during an outbreak in the North Eastern region of India: peculiarities in clinical presentation, laboratory findings and complications; Indian J Pediatr. 2011;78 (11) :1365-70
18. Veena Mittal, Naveen Gupta, Dipesh Bhattacharya, Kaushal Kumar, R.L. Ichhpujani, Sharda Singh, Mala Chhabra,,U.V.S. Rana; Serological evidence of rickettsial infections in Delhi; Indian J Med Res. 2012l; 135(4): 538–541.
19. Raoult D, Drancourt M. Antimicrobial therapy of rickettsial diseases. Antimicrob Agents Chemother. 1991;35(12):2457-62
20. Purvis JJ, Edwards MS. Doxycycline use for rickettsial disease in pediatric patients. Pediatr Infect Dis J. 2000;19(9):871-4