Case Report

Rickettsial meningoencephalitis in a child—A case report

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Summary

Severe central nervous system involvement has been reported in adults with *Rickettsia conorii* infection but rarely in children. We report here a serologically documented case of meningoencephalitis in a child caused by spotted group *R. conorii*. Rickettsial infection is a relatively under-diagnosed entity in children with fever and rash, probably due to low index of suspicion and the lack of definitive diagnostic facilities. Rickettsial infections can be treated effectively with anti-microbials; if they remain undiagnosed and untreated, they are associated with significant morbidity and mortality. This differential diagnosis should be considered when a child is seen with fever and rash.

Key words: Rickettsioses, Meningitis, *Rickettsia conorii*, Indian Tick Typhus, Tick.

Introduction

Spotted fever group *Rickettsiae* are Gram-negative intracellular bacteria associated with arthropods, mainly ticks, as vectors. To date, only 12 tick-borne rickettsioses are recognized worldwide. Indian tick typhus (ITT) is a tick-borne rickettsioses prevalent in India [1]. Severe involvement of the central nervous system (CNS) has been reported in adults with *Rickettsia conorii* infection [2, 3], but rarely in children [4, 5]. We report a serologically documented case of meningoencephalitis in a child caused by spotted group *Rickettsia*. The following case history is reported because of the importance of diagnosing this manifestation of *Rickettsia*, for which there is effective treatment.

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Case Report

A 4-year-old, previously healthy girl child was admitted to Dr Bidari's Ashwini Institute of Child Health and Research Centre, Bijapur, with 7 days history of fever and one episode of generalized tonic–clonic convulsions and altered sensorium of 1-day duration. She had developed rash over the face and limbs 3 days following the onset of fever. Physical examination on admission revealed a temperature of 101°F. There was maculopapular rash over the face and both extremities involving palms and soles. There was oedema of hands and lower limbs. There was no lymphadenopathy, conjunctivitis, eschar or ear discharge. Liver was 4 cm and spleen was 3 cm below the costal margins. She was delirious with no cranial nerve palsy or focal neurodeficits. There was no evidence of papilloedema on fundoscopy. There was history of presence of many stray dogs with tick infestation around her residence, but no definite history of tick bite

On investigation, haemoglobin was 8 gm%, leucocyte count 16 600 mm^{-3} with 79% polymorphs and 16% lymphocytes and platelet count was 17 000 mm^{-3}. Peripheral blood smear for malarial parasites and Widal test were negative. Blood sugar was 140 mg/dl and serum electrolytes were normal. Serum ALT was 110 U/l. Examination of CSF sample obtained by lumbar puncture revealed a white blood cell count of 180 cells/mm^3 with 12% polymorphs and 88% lymphocytes, a glucose level of

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70 mg dl^{-1} and a protein concentration of 85 mg dl^{-1}. Stains and cultures for bacteria, mycobacteria and fungi were all negative. A cranial computed tomographic (CT) scan was normal. The patient was started on ceftriaxone (100 mg kg^{-1} day^{-1} in two divided doses) intravenously; and in view of characteristic rash and its distribution, possibility of rickettsial infection was considered and child was started on chloramphenicol (75 mg kg^{-1} day^{-1} in four divided doses) and tab doxycycline (two loading doses of 2.2 mg kg^{-1} $dose^{-1}$ at 12-h intervals followed by 2.2 mg kg^{-1} $24\,h^{-1}$ divided 12 hourly through feeding tube). Her serum was sent for Weil-Felix test, which was found positive at a dilution of 1:640 for OX 2, while OX 19 and OX K were negative (Plasmatec, Bridport Dorset, UK). Meanwhile, paired serum samples collected 2 weeks apart were sent to Viral & Rickettsial Zoonosis branch of Centre for Disease Control & Prevention Atlanta, for rickettsial antibody testing by indirect immunofluorescence assay. Child's general condition and sensorium gradually improved over 1 week. Chloramphenicol and doxycycline were continued for 10 days with the monitoring of complete blood counts. The child's paired serum specimens tested positive for *R. Conorii IgG* with titres of 512 and 8192, respectively (more than 4-fold rise) by indirect immunofluorescence assay.

Discussion

Rickettsiae derive their name from the American researcher, Howard Ricketts, who discovered them in 1909 in Montana, USA, as the source of a serious disease [Rocky Mountain spotted fever (RMSF)]. He himself died from typhus in an epidemic in Mexico some years later. *Rickettsiae* multiply intracellularly. They have a Gram-negative cell wall structure, but cannot be detected by Gram staining, although they can be by Giemsa staining but with difficulty.

The cases of rickettsial infection have been documented mainly from South India [6–9]. The *R. conorii* was first described by Conor in 1910. In September 1932, at the First International Congress of Mediterranean Hygiene, the name Mediterranean spotted fever was adopted. Other names given to this illness are Boutonneure fever, Kenya Tick-Bite Fever, African Tick Typhus, Indian Tick Typhus, Israeli Spotted fever and Marseilles fever, depending on the region [10]. *Rickettsia conorii* is an obligate intracellular parasite of Ticks. In Mediterranean area, the vector is the brown dog tick *Rhipinecephalius sanguineus*, but other species of mites may act as vectors in other geographic areas [11]. Rickettsias are wide spread in ticks and can parasitize many of their organs including ovaries, and hence can be transmitted transovarially. Thus ticks are not only vectors but also reservoir of infection; therefore physical contact with dogs is not necessary.

The initial bite passes unnoticed and in many cases the primary lesion/inoculation scar (Tache noire) is not always present as in our case. The onset of disease is usually abrupt with headache, malaise and fever, lasting for 6–12 days. Generalized myalgia, especially involving leg muscles and joint pain, is a prominent feature. The rash usually develops between 3rd and 5th febrile day with initial lesions appearing on extremities and spreading to trunk, neck, face, buttocks and palms in 24–36 h. The lesions are macular or maculopapular and may be purpuric. Our patient had maculopapular rash with characteristic distribution. Severe involvement of CNS has been reported in adults with *R. conorii* infection [2, 3], but rarely in children [4, 5]. Children present with various degree of impaired consciousness, delirium and convulsions. Neurologic sequelae have been observed. Our patient had clinical and cerebrospinal fluid findings of meningoencephalitis. Other complications like pneumonia, myocarditis, acute respiratory distress syndrome, acute renal failure and disseminated intravascular coagulation have been reported.

Rickettsia conorii cannot be isolated from blood culture by routine laboratory procedure. The clinical features, geographic background and epidemiological considerations help to establish diagnosis. Laboratory diagnosis is an important adjunct and involves serologic identification of serum antibodies [12]. Diagnosis of rickettsial infection is mainly by serologic methods [13]. Indirect immunofluoroscent assay is the reference diagnostic method for rickettsial infection, but cross-reacting antibodies of related isolates confound interpretation of the results and it becomes positive only in late phase of disease [14]. Our patient's serum tested positive for *R. conorii* by IFA done at Centers for Disease Control and prevention (CDC), Atlanta. Western blot test is more sensitive than IFA test, and it is frequently positive in acute phase sera when antibodies cannot be detected by IFA [15]. Our child's serum tested positive for Weil Felix Test (WF) at a dilution of 1:640 for OX 2. WF is inexpensive and can be performed rapidly to substantiate the diagnosis. However, low sensitivity of WF is a problem [16]. Even though the sensitivity of WF has been claimed less, there are several reports suggesting good correlation of WF Test with other standard tests used [17, 18]. In the study conducted in South India [19], the sensitivity of patient's antibody was 30% at a titre break point of 1:80, but specificity and positive predictive value were 100%. Some authors have suggested that even though WF test is not a very sensitive test, it is quite a specific test when it is positive [20]. Thus WF test may be the only serological test available in developing countries like India. It can be used in confirming a tentative diagnosis of rickettsial fever mainly during acute

phase of the disease when specific therapy can be life saving.

Doxycycline is the drug of choice. Other drugs are tetracycline, chloramphenicol, ciprofloxacin, azithromycin and clarithromycin [21]. Although tetracycline should not be used in children <8 years, the rational for their use in this setting is as follows: (i) staining of teeth by tetracycline is dose-related and unlikely to occur in association with one or two short courses of therapy; (ii) doxycycline is less likely to stain developing teeth than the other tetracyclines, possibly because it binds less to calcium; (iii) doxycycline is also the drug of choice for early ehrlichiosis, which can be confused with other rickettsial infections [22]. The optimum duration of specific therapy has not been definitely established and different antibiotic regimens ranging from single dose to treatment for up to 15 days have been recommended [23]. As our patient was critically ill and CNS was involved, we used both doxycycline and chloramphenicol for 10 days with which the child recovered well.

In summary, early diagnosis of rickettsial infections is important, as these can be treated with inexpensive antibiotics and can be fatal if untreated. The availability and the cost of standard serological methods for *Rickettsia* are the major problems in developing countries like 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 WF.

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