nervous system.[7] Tsutsugamushi is the rickettsia with the meningeal involvement. CNS complication is widespread and includes the infarction, cerebellitis, hemorrhage, encephalitis demyelination, subdural hematoma, and meningitis. These may manifest as altered sensorium, restlessness, motor weakness, seizures, meningism, and cranial nerve deficits.[7] The rickettsia directly invades the CSF. A prospective study of Thai children revealed that scrub typhus was the second most common cause of aseptic meningitis next to Japanese encephalitis.[13] None of our patients had a repeat CSF study due to serological diagnosis and clinical recovery within 72 h.

Weil–Felix test (OX-K) was considered positive with the titers of 1:160 or more in the present study based on manufactures' guidelines and cut off used in some other studies elsewhere.[14] Furthermore, there are no epidemiological studies done from this region for establishing such cut-offs. Other studies from India have taken a cut off of as low as 1:80 as positive while still others have demonstrated that a cut off >1:320 indicates a definitive diagnosis of scrub typhus.[11] Most of western literature have advised against performing this test for diagnosis of rickettsial infection.[15] The poor sensitivity is now well demonstrated, but indirect immunofluorescence antibody assay and indirect immunoperoxidase require highly trained personnel and production of antigens may vary among different laboratories, leading to inconsistencies in the interpretation of results.[16] WFT can be used as a screening test. It helps to detect more cases than misdiagnosed ones and when positive is reasonably specific. In spite of all these drawbacks, WFT still serves as a useful and affordable diagnostic tool for laboratory diagnosis of rickettsial diseases in resource-poor countries. Isaac *et al*.[17] have demonstrated that the sensitivity of WF test was 30% at the breakpoint titer of 1:80, but the specificity and positive predictive value were 100%. Evaluations done in different laboratories have showed that this test had a specificity of over 98% and a sensitivity of about 43%.[18] In several areas around, the world, WF test has proved useful in documenting the presence of these infections for the first time[19] Hence, WF test is still not entirely obsolete in resource-limited parts of the world and has to be interpreted in the correct clinical context.[20] as done in the present study. Primary infection produces a rapid rise in IgM antibodies within 8 days, whereas secondary or reinfection is characterized by a sharp rise in IgG levels, with a variable IgM response. Since ICT also detects IgG antibodies, the patient may have had a secondary infection and thus the positive result. It has been suggested that recombinant antigen-based ELISA is suitable in moderately equipped laboratories in the scrub typhus endemic regions.

Subacute onset of meningitis like TBM is also considered an additional diagnostic challenge. Both TBM and scrub typhus meningitis showed picture of lymphocyte-predominant CSF. Adenosine deaminase (ADA) >10 increases the probability of TBM.[21] on the contrary, slightly decreased CSF glucose and presence of focal signs in TBM may help in differentiating it from scrub typhus meningitis.[2] In addition, the elevated transaminases tend toward scrub typhus infections, which would be not so usual in TBM unless they were already on treatment.[2] CSF Adenosine deaminase (ADA) levels for our patients were less than 10 U. Hence, ADA levels may be helpful in differentiating scrub meningitis from TBM but more studies are necessary to confirm. Rifampicin is alternatively used to treat severe scrub typhus. Presence of lymphocytic CSF in a given patient, with improvement following antituberculous therapy (ATT), may mask the diagnosis of scrub typhus.[7] Recovery in meningoencephalitis is fast with appropriate therapy. All neurological abnormalities in our study recovered within 3–7 days of doxycycline therapy. Doxycycline remains the drug of choice. All patients responded well. There was no death due to meningitis which can be explained by the fact that the authors had high index of suspicion as this was a prospective study. Accordingly, necessary investigations were sent at the earliest leading to early diagnosis followed by institution of appropriate therapy. The major limitation of this study is small sample size of the study and the inability to do a confirmatory test in all cases due to nonavailability of the test in our Institute and the high cost of performing the same from private laboratories.

Conclusions

Scrub typhus is a re-emerging cause of acute and subacute meningitis, which can be difficult to diagnose. The eschar, a path gnomonic clinical feature, is often not present, and as the larval bite is painless, a history of insect bite is unlikely to be solicited from the patients. Due to the presence of lymphocytic pleocytosis with increased CSF protein; TBM is a close differential diagnosis. Hence, misdiagnosis may lead to unwarranted prolonged empirical antituberculous therapy in cases of lymphocytic meningoencephalitis. Diagnosis of scrub typhus meningitis is important as it is treatable with inexpensive antibiotics and if left untreated, can be potentially fatal. The highlight of this study is that it is the first, prospective study of scrub meningitis from northeastern region of India. What is noteworthy in this study that the WFT can still be fruitful for diagnosing this disease in a resource-limited setup? Our study, however, is limited by its size, and further research, on a larger scale, is warranted for this potentially fatal disease.

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