Rickettsial Diseases in India: Not as Uncommon as Believed

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Till about ten years ago traditional teaching was that rickettsial diseases (Typhus and Spotted Fever groups) were rare in the country. Initial descriptions were from soldiers in the Assam and Burma fronts during the Second World War\(^1\) when it was a problem second only to malaria. After that, there was little data from the country and it was generally believed that the problem was a medical curiosity. So, much so that tests for rickettsial diseases including the Weil Felix were available in only a few centres. Consequently, the next generation of tests like complement fixation (CFT), immunofluorescence assay (IFA) and microimmunofluorescence (MIF) were never available in India. In the last decade there have been increasing reports in this journal and others that have clearly shown that Scrub Typhus and the Spotted Fever group of illnesses occur in most regions of the country.\(^2\)\(^-\)\(^7\) The clinical presentation can range from a short duration undifferentiated fever to a PUO to one with multiorgan dysfunction with significant morbidity and mortality.\(^8\) Part of the explanation for the wide variation in clinical presentations is that there are strain variations in *O. tsutsugamushi* and that this in part contributes to the varying degree of virulence seen with the organism.\(^8\) Though one would have logically considered Scrub typhus to be a rural disease; it is well described from urban areas like Delhi\(^9\) and Bangkok and can present in people from towns and cities as there can be small ‘mite islands’ in vegetation around residences.

It is not only scrub typhus that is prevalent in India. Seroprevalence studies in areas like Delhi, Central and South India have shown evidence of *R. conorii* infection.\(^5\)\(^-\)\(^10\) Clinical cases of spotted fever are well described.\(^11\)\(^-\)\(^12\) Surprisingly there are more descriptions of this condition in children when compared to adults.\(^13\) A sero-survey in Delhi done by the National Centre for Disease Control in patients with PUO showed 8.2% positivity for rickettsial disease using the Weil Felix in a series of 737 cases. When the test was looked at in those with clinically suspected rickettsial disease, it was positive in 33.3%. In this sub-group, results suggested scrub typhus in 48.2%, spotted fever in 27.5% and typhus group in 6.8%.\(^9\)

As rickettsiae are difficult and dangerous to grow, most laboratories in the country use the Weil Felix for the diagnosis of rickettsial illnesses. This is considered an insensitive test in most parts of the world and one which is not very specific. Studies from India\(^14\)\(^-\)\(^16\) have reported that sensitivity and specificity are reasonable when done in the second week of illness. The IgM and IgG ELISA’s are more sensitive and specific. However, as the kits are imported it is available in very few centres in the country. Other standard tests like IFA are most often unavailable. PCR of the 56 kd outer membrane antigen particularly from the eschar and the blood have had reasonable yields in the hands of laboratories interested in the condition. The problem with all antibody tests is that they ideally require a demonstration of a four-fold rise in titre. This is not practical in most clinical situations. A positive antibody test on its own means little, if a group of healthy local population has not been screened and the background level of activity determined. A single positive test can only be given some significance if the titres are at least > 2 standard deviations more than the background healthy population level. A cut-off level determined in another geographical

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area cannot be arbitrarily used at a different location. Other common febrile illnesses of the area have to be excluded clinically and with appropriate tests. It is not an uncommon scenario to see reports of positive typhoid, leptospira and scrub serologies in the same patient highlighting the limitations of serological tests done at a single point of time. In view of the wide spread prevalence of rickettsial disease now documented in India; it is high time that the more sensitive and specific ELISA tests for both Scrub typhus and Indian tick typhus are made widely available. A rapid point of care screening card test also needs to be developed.

Doxycycline is usually the drug of choice for both scrub typhus and spotted fever. It can almost be used as a therapeutic test in suspected febrile rickettsial disease as a clinical response usually occurs in 48 hours. Early recognition and therapy clearly decreases both morbidity and mortality. In sick patients with multiorgan dysfunction, IV doxycycline is the preferred route of therapy. Paradoxically as the drug is cheap, no IV preparation is available in this country and we have to rely on the oral route. The Government of India needs to ensure that this relatively cheap drug is made available for intravenous use. A meta-analysis done in China showed that Doxycycline was the most rapidly acting drug. In pregnant patients, Azithromycin is the current drug of choice. Chloramphenicol is another useful agent in rickettsial diseases which is less used nowadays in view of its potential toxicities.

Vaccine work has been ongoing for many years as scrub typhus was an important cause of morbidity in both the Korean and Vietnam wars. However, as of now there is no reliable vaccine with long duration protection available.

References