Commentary: Tick talk: A glimpse into the literature

Since its first report in 1977 in the town of Old Lyme, Connecticut, United States, there has been a consistent increase in the prevalence of Lyme disease worldwide. The seroprevalence of the disease remains remarkably variable worldwide—varying by country and region in the same country. Though relatively sparse and sporadic, there is an increase in reports of Lyme disease from various parts of India.[1,2] There is a paucity of epidemiological data on infection due to *Borrelia burgdorferi*, and the risk factors for contracting the illness in India have remained largely unknown. There are two studies that estimated the prevalence of antibodies against *Borrelia burgdorferi* in the Indian population. Using commercial enzyme-linked immunosorbent assay (ELISA) kit to detect IgG antibody to *Borrelia burgdorferi*, Praharaj *et al*.[2] estimated seroprevalence of 13% in northeastern states of India. In this issue of the journal, Babu *et al*.,[3] estimated the seroprevalence of 15.6% *Borrelia burgdorferi* infection by a two-tier approach—using an ELISA initially, followed by specific Western blot as a confirmatory test in Nagarahole and Bandipur forest ranges in South India.

The diagnosis of Lyme disease remains elusive. In majority cases, a combination of pathognomonic erythema migrans rash, travel history to an endemic area, clinical findings, and supportive serological investigations have been described to clinch the diagnosis. In the first few weeks of the illness, the serological test may be negative as antibodies against *Borrelia burgdorferi* are slow to develop. IgM usually takes 1 to 2 weeks to appear in the blood and IgG may not be detectable up to 4 to 6 weeks of infection.[4] However, once produced in response to *Borrelia burgdorferi*, IgM and IgG persist for a long time, thereby, making serology difficult to differentiate between old and new infections. The Centers for Disease Control and Prevention (CDC, USA) and the Food and Drug Administration (FDA) in 1995 recommended a two-step algorithm—using an enzyme immunoassay initially and if reactive or equivocal, then a Western blot to run on the same sample to confirm the serodiagnosis.[4] A study from the United States estimated the huge economic burden involved with the serological tests for Lyme disease; the study concluded that these tests are being overused and only 12% out of 3 million tests yielded a positive result.[5] CDC recommends performing serological screening for Lyme disease only in symptomatic patients with a risk of exposure to ticks.[4] Recently CDC recommended a modified two-test method on July 29, 2019, which uses a second ELISA test rather than a western blot in Lyme disease serological test algorithm.[6]

The diagnosis of ophthalmic manifestation of Lyme disease in the absence of systemic symptoms and suggestive history is challenging. Usually, the ophthalmic manifestations are reported in later part of the illness and there are possibilities of negative serological tests.[7] There are only two available reports of ophthalmic involvement in Lyme disease from India and both had presented with neuroretinitis.[8,9] One patient was an inhabitant of Nagarahole forest and had a history of a tick bite, although there was no history or presence of classic erythema migrans like skin rash.[8] The second patient had a history of a recent visit to hilly terrain in the Himalayas and had denied any of tick bite or any other systemic manifestation.[9] In both cases, a diagnosis of Lyme disease was achieved as a disease of exclusion—serological tests and from a suggestive history.[8,9]

One needs to interpret data on seroprevalence with caution; higher seroprevalence does not necessarily mean the increased incidence of the disease.[10,11] Many of these studies on the seroprevalence of Lyme disease had asymptomatic seropositive subjects. We do not know whether asymptomatic seropositive subjects are at risk of developing symptomatic disease or represent late sequelae of infection, and what are the chances of seroreversion in them. Fahrer *et al*.[10] found no increased risk for the development of symptomatic disease in asymptomatic seropositive subjects up to 6.5 years of follow-up. Chances of ocular involvement will be rather rare in such scenario. Ocular involvement is considered to be less than 1% in patients with Lyme disease and remains the cause of less than 1% of all uveitis cases in an endemic country.[7,12] Because of the low prevalence of Lyme disease in uveitis, even the two-tier approach of serological testing is not considered sufficient to establish a diagnosis.[13]

In conclusion, though rare in India, one should consider a diagnosis of Lyme disease in uveitis patients based on systemic findings, history of a tick bite, especially if the patient hails from a forested area or gives a history of travel to an endemic area. Serological testing should be used accordingly, and the diagnosis of Lyme disease remains a diagnosis of exclusion.

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