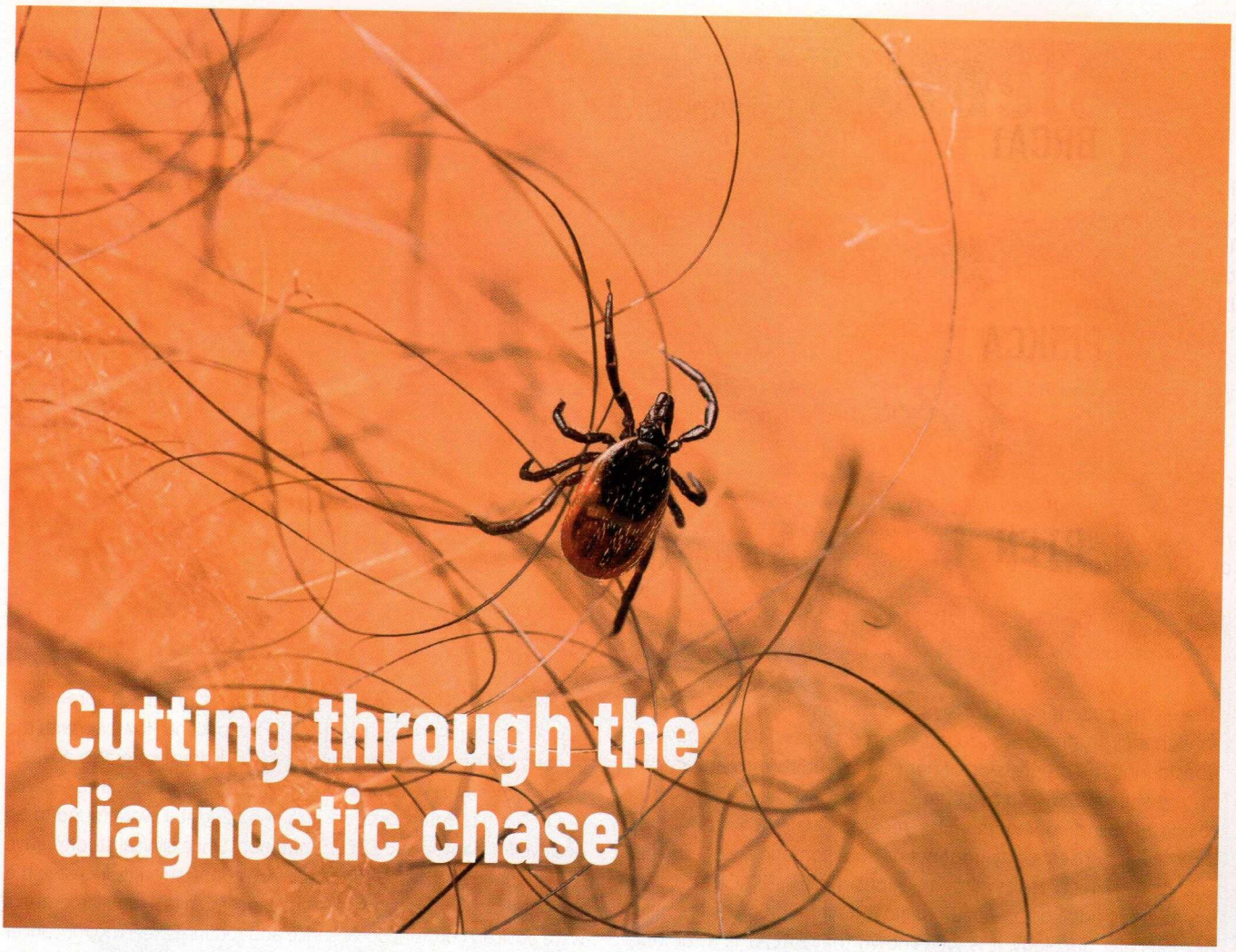

Cutting through the diagnostic chase

A report highlighting the need for prompt interventions in Rikettsia

On a trip to Benaras, a 44-year old male developed a fever with chills. Seven days later, as he returned to Mumbai, he was drowsy and unresponsive, and had convulsions at the airport. He was immediately admitted to Hinduja Healthcare, one of the leading hospitals in Khar, Mumbai. The doctors were unable to diagnose his condition with the non-specific clinical manifestations of fever and rash. As the patient's condition worsened, the intensivist sent an EDTA whole blood sample for a molecular diagnostic assessment for the comprehensive CNS panel, and endotracheal secretion for the atypical pneumonia panel. Within 8 hours, the lab was able to identify Rickettsia in the blood sample. Unfortunately for this patient, the diagnosis was too late, and he succumbed to the infection the same day. Had the patient been able to avail of quality diagnostic testing earlier, he would have been appropriately diagnosed and treated in time.

Rickettsial infections are caused by nonmotile, gram negative pleomorphic bacteria belonging to the genera Rickettsia. These bacteria are obligate intracellular parasites that grow in the alimentary canal of arthropods such as fleas, ticks, and lice. These arthropods

can act as both vector and reservoir, and infect humans primarily via infected saliva while biting or via infected vector feces getting into the bite wound. From the bite wound, the bacteria multiply at the site of entry and enter the blood stream, finally localizing in the vascular endothelial cells and resulting in thrombosis and eventually necrosis and lysis of the endothelial cells. Once released, they infect the surrounding healthy cells; and the cycle continues.

Diagnosis of Rickettsia can be extremely challenging as the initial clinical manifestations are non-specific and tend to mimic other common viral infections. Fever with chills, headache, myalgia, rash, and sometimes eschar are the common clinical features. Some of the known reliable diagnostic tests include serologic detection of antigen via immunofluorescent assay or antibody by the Weil-Felix test. Once diagnosed, treatment with doxycycline should be started immediately, the earlier the better. Left untreated, Ricksettsial infections can result in death.

Since the patient in this case presented with a non-diagnosable fever and rash, a condition that was worsening, the intensivist considered molecular testing as a quick and last resort. The sensitivity or limit of detection of molecular-based assays is as low as 102-103 colony forming units/mL of blood and is dependent on identifying DNA of the pathogen. "Doctors can either request for certain panels to be tested based on the clinical symptoms and expected differential diagnosis, or may confer with our diagnostic team", says Dr Aparna Kotekar, HOD, Molecular Department, iGenetic Diagnostics in Mumbai. "Doctors can also confer with us as to what sample to provide for the diagnosis. A localized sample is likely to give clearer results, and a cerebrospinal fluid sample would have been preferred for the comprehensive CNS panel testing". However, this was not possible in this case, and the doctors were only able to provide a more easily obtainable sample of blood. Endotracheal secretion sample was provided for the atypical pneumonia panel which includes unusual bacteria in the hope of covering more probable pathogens. Dr Kotekar found this case to be particularly interesting as the comprehensive CNS panel testing was able to detect Rickettsial infection from the blood without necessitating a cerebrospinal fluid sample. Molecular diagnosis played a significant role in identifying the pathogen in a short period of time, especially since any microbial cultures would have come back negative as Rickettsia is an obligate intracellular parasite that cannot be grown in culture media. A cell culture is required for their identification which would take several days before a confirmed diagnosis would have been possible. Unfortunately, even though the doctors were already considering Rickettsial infection as a potential diagnosis and had started the patient on doxycycline in addition to other antibiotics as they awaited the results from the molecular testing, and took all the correct and necessary measures for a quick differential diagnosis, the results came too late for the patient. While Rickettsia does have high mortality rates when left untreated, it is fairly easy to treat if diagnosed in time. Early diagnosis remains to be one of the major concerns with Rickettsial infections due to the non-specific clinical symptoms. Now however, if timely quality healthcare is available, there are molecular diagnostic assays that can quickly screen through panels of probable causative agents and assist in deciding the course of a much-needed early therapy ◪

- Dr Shivanee Shah