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LETTER TO THE EDITOR / EDİTÖRE MEKTUP

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Beyond Crimean-Congo Hemorrhagic Fever: Are Overlapping Tick-borne Pathogens Being Overlooked in Endemic Regions?

Kırım-Kongo Kanamalı Ateşi'nin Ötesi: Endemik Bölgelerde Kene Kaynaklı Diğer Patojenler Gözden Kaçıyor mu?

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Dear Editor,

Crimean-Congo hemorrhagic fever (CCHF) is an infection that exerts a significant impact during spring and summer months across a broad area encompassing the Central Anatolia, Central Black Sea region, and Eastern Anatolia in Türkiye, occupying a major place on the regional healthcare agenda due to its associated mortality. This infection, in which *Hyalomma marginatum* ticks generally serve as vectors, can also be transmitted through contact with infected animals and humans. Following tick exposure and removal, and after an incubation period, an assessment by an infectious disease specialist is performed when non-specific symptoms (such as fever, fatigue, myalgia, nausea, and diarrhea) and laboratory findings including thrombocytopenia, leukopenia, and elevated transaminase levels are present[1]. It is suggested that CCHF fatality rate may remain relatively low in endemic regions when clinicians possess a high level of awareness regarding measurable parameters, such as elevated transaminase levels and the severity of thrombocytopenia. In this context, the CCHF fatality rate in Türkiye was reported as 3.4% in 2024[2]. At this point, the primary question the clinician seeks to answer is whether they are dealing with a case of CCHF, given that it is an infection capable of producing a rapid and dramatic clinical trajectory with a considerable mortality rate. However, CCHF is not the sole infection transmitted by ticks. This prioritization, established in the interest of patient welfare, leads to the oversight or diagnostic delay of other potential tick-borne infections or co-infections in a subset of cases.

It should be noted that tick-borne pathogens present in Türkiye also include *Borrelia*, *Rickettsia*, and *Babesia* species, as well as *Francisella tularensis* (*F. tularensis*)[3]. The fact that *Borrelia*, *Rickettsia*, and *Babesia* species are found in Central Anatolia and its surroundings, while *F. tularensis* is found in the Black Sea region, clearly broadens the differential diagnosis of tick-borne infections in the endemic regions of CCHF located at the intersection of these different climatic zones[3,4]. *Coxiella burnetii* and tick-borne encephalitis virus can also be appended to this list[5]. In *Anaplasma* and *Ehrlichia* infections, the presentation of

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thrombocytopenia, leukopenia, and elevated transaminases closely mimics CCHF, as does Q fever, which manifests with non-specific flu-like symptoms accompanied by the same laboratory findings. Similarly, although Lyme disease can be distinguished by the presence of a typical rash, its signs and symptoms remain among those diagnoses that may be overlooked in a clinical setting excessively focused on a provisional CCHF diagnosis[6-8].

In cases of tick bite, individuals may remove the tick themselves, or the removal is performed by a healthcare professional at a medical facility. In either scenario, narrowing the differential diagnosis list is generally not possible, as the attached tick species cannot be definitively identified and, exceptionally transmission can occur via tick species other than the primary vector. In patients with a history of tick bite presenting with compatible signs and symptoms, treatment targeting other potential pathogens should not be delayed while awaiting laboratory confirmation. Empirical treatment, such as doxycycline for non-pregnant adults without contraindications which covers *Borrelia*, *Coxiella*, *Anaplasma* and *Rickettsia* infections, can be initiated prior to receiving test results[8,9]. At this point, in cases where the CCHF polymerase chain reaction result is negative, laboratory parameters show atypical course, or symptomatic improvement is delayed/does not occur, it is important to request molecular and serological tests for alternative diagnoses without delay, and to consider empirical treatment when necessary.

Sincerely,

Footnotes

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