Commentary

Singh RK *et al*. have published a useful paper about intracranial hemorrhage in a patient coinfected with dengue and leptospirosis.[1] There are some comments which may explicit benefits of this paper in more details.

Zoonoses have been on top of list of the emerging infections recognized during the past decade. Leptospirosis and dengue fever (DF) are two zoonotic infectious diseases with nearly similar clinical manifestation and high probability of coinfection. There are some challenges in diagnosis and care giving to patients who suffer these diseases separately or having both of them at the same time. Similarity of symptoms, indistinct not fully explained pathogenesis, and insufficiency of rapid test kits are the most important challenges.

Dengue virus (DENV) causes diseases ranging widely in severity, from self-limited DF, to life-threatening dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS). Dengue is the most rapidly spreading vector-borne viral disease in the world with about 100 million cases annually worldwide. Epidemiology of DF, DHF, and DSS with climate change and the convenience of travel is fast changing and in recent decades, a steady increase in the number of severe dengue cases has been seen. In the last decades, incidence has increased 30 times with increasing geographical expansion to new regions and spreads from rural to urban areas. Approximately 2.5 billion human (one of each three people) live in dengue endemic countries. Studies showed that 50% of dengue cases may be misdiagnosed, as a result of inaccurate evaluation and assessment of the signs and symptoms of patients.[2,3]

Despite its growing pattern, pathogeneses are not clearly understood and the mechanisms remain unclear. Vascular leakage, thrombocytopenia, and hemorrhage are the major clinical manifestations associated with severe DENV infection. Now, there are some hypotheses like virus virulence, antibody-dependent enhancement, and IFN/TNF-mediated immunopathogenesis. Aberrant activation of T cells, overproduction of soluble factors, cytokine overproduction, infection of endothelial cells, apoptosis caused by hepatocytes, molecular mimicry between DENV proteins and host proteins, and activation of coagulation and fibrinolysis systems after dengue virus infection are proposed but they are insufficient to explain clinical manifestations of DHF/DSS such as thrombocytopenia and hemoconcentration. Vasculopathy, coagulopathy, and unbalance between coagulation and fibrinolysis activation are induced by DENV that is involved in the pathogenesis of hemorrhage.[3,4]

Almost always, severe dengue disease is presented in individuals that have pre-existing immunity against heterotypic DENV subtypes and in infants whose mother has low levels of dengue antibodies.

Leptospira is a spirochete, of which human is an accidental guest, and can survive in humid or warm environments, alkaline floor, kidney of infected animals, and water. Leptospirosis considered as the most common zoonosis in the world (500,000 are registered annually worldwide) and present in urban and rural areas and close contacts with infected environments and animals have key role in this disease and promoting its development.[2,5]

Infected patients may remain asymptomatic in most of the cases or develop disease, which may become acute

or chronic; in its acute form, the symptoms may be undifferentiated or very mild or be present in a severe way, as a consequence of extensive vasculitis, known as Weill syndrome and that is characterized by liver and kidney damage or pulmonary hemorrhage commonly leading to death. Leptospirosis is one of the world's most prevalent zoonoses, with a clinical picture varying from a mild to potentially life-threatening disease in which hemostatic derangements play a central role. Despite these facts, leptospirosis is a neglected disease, which explains why many crucial aspects concerning its pathogenesis remain unanswered.[5,6]

The pathogenesis of leptospirosis is not completely understood. In the septicemic animal models, vascular injury is detected in various organs. In the walls of vessels, spirochetes can be found. The exact mechanism of vascular damage is not clear. The toxic effect of the *Leptospira* has been proposed to cause directly the vascular injury, but bacterial endotoxin has not been demonstrated.[2,6]

During the illness, in the second phase, immune complex deposition and other host's immune response may play a role in endothelial injury. During septicemic phase, invading Leptospiras are distributed throughout the body. Penetration and invasion of tissues is presumably accomplished through a burrowing motion produced by a pair of axial filaments and release of hyaluronidase. Kidney, liver, brain, lung, and meninges are the main organs that are affected. A systemic illness will appear due to dissemination of proliferated spirochetes in tissues, which has a broad spectrum of clinical manifestation. Ecchymosis and petechiae will occur in most internal organs in a severe case.[5,6]

In leptospirosis, systemic vasculitis with endothelial injury is seen microscopically. The damaged endothelial cells usually show different degrees of swelling, necrosis, and denudation.[6]

The challenges are as follows:

- Regional overlap of epidemic area of dengue on leptospirosis area.
- Similarity of pathogenesis mechanism and clinical signs and symptoms.
- Lack of adequate information about them in health workers.
- Lack of sufficient rapid diagnostic kit for diagnosis.
- Completely different treatment for these diseases.
- Increasing number of patient during last decades.
- Climate changes and prepared condition for spreading of diseases.
- Lack of any effective and sufficient vaccine for dengue and leptospirosis.

Recommendation

Health workers should know some key point for differentiating:

- In dengue, hem concentration because of plasma leakage is present, but in leptospirosis this problem is not seen.
- Despite dengue, liver enzymes in the leptospirosis rarely increase more than 300 IU.
- In patients with elevated liver enzyme (more than 300 IU) with increased hematocrit and positive MAT for leptospirosis, dengue coinfection should be considered.

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References

1. Singh RK, Ghatak T, Baronia AK, Garg P. Intracranial hemorrhage in a patient co-infected with Dengue and leptospirosis. J Neurosci Rural Pract 2013;4:366-67.
2. Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases: Expert consult premium edition-enhanced online features and print (Two Volume Set). In: Mandell GL, editror. 7th ed. New York: Churchill Livingstone, Inc.; 2010. p. 206.
3. Lei HY, Yeh TM, Liu HS, Lin YS, Chen SH, Liu CC. Immunopathogenesis of dengue virus infection. J Biomed Sci 2001;8:377-88.
4. Behera B, Chaudhry R, Pandey A, Mohan A, Dar L, Premlatha MM, *et al.* Co-infections due to leptospira, dengue and hepatitis E: A diagnostic challenge. J Infect Dev Ctries 2009;4:48-50.
5. Dircio Montes Sergio A, González Figueroa E, María Saadia VG, Elizabeth SH, Beatriz RS, Altuzar Aguilar Víctor M, *et al.* Leptospirosis prevalence in patients with initial diagnosis of dengue. J Trop Med 2012;2012:519701.
6. Babamahmoodi F, Babamhmoodi A. Recovery from intracranial hemorrhage due to leptospirosis. Case Rep Med 2011;2011:504308.

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