

AN OVERVIEW ON DENGUE HEMORRHAGIC FEVER

Prasit Futrakul, M.D.*

Two decades has elapsed since the first epidemic outbreak of hemorrhagic fever occurring in 1951, which has already claimed many thousand lives of Thai children.⁽¹⁾ A campaign launched against this entity in the early part of last decade discovered that the responsible organisms were Dengue and Chikungunya viruses.⁽²⁾ Earlier two hallmarks embarked by the hematologists as well as clinicians were as follows^(3, 4) (I) increased vascular permeability during the active phase of disease which was substantiated clinically as rising of hematocrit, hypovolemia, oliguria and pathologically as internal accumulation of extravasated plasma (II) bleeding diathesis and thrombocytopenia manifested externally as skin petichiae, purpura, epitaxis or internally as gastro-intestinal hemorrhage and in rare occasions which was usually associated with extremely severe form, as cardiopulmonary hemorrhage. These puzzling observations had focused everyone's interest. An enthusiastic era of investigations and researches of the last decade had been advocated to studying the plausible triggers and mechanisms of increased vascular permeability and bleeding diathesis associated with thrombocytopenia, of which forms series of the vital topics to be presented somewhere in this special issue

Recent studies of several investigators indicated that there was an initial depletion of complement profiles.^(5,6) The impression at present, favors mainly consumptive process of the complement

although other possibilities namely leakage of the complement extravascularly or inhibition of complement production may play some minor adjunctive role.⁽⁷⁾

Concomittent to this observation, evidence of platelet consumption was also revealed in the platelet survival study of Poshyachinda, M⁽⁸⁾ who demonstrated the markedly short platelet-survival time, in conjunction with the decreased number of circulating platelets during the active phase of dengue hemorrhagic fever. Furthermore, the degrees of consumption of both the complement and platelets correlated well with the clinical severity; thus suggest their spatial relationship to the pathogenesis of the disease.

Inasmuch as various mediators may be released from such activations of both complement and platelets namely anaphylatoxin, chemotaxis of the former and histamine, serotonin, permeability factor of the latter, the mechanisms of increasing vascular permeability may then be implicated. As speculated, depletion of Hageman-factor demonstrated by Mitrakul⁽⁸⁾ provides another possible clue of activating the alternative intermediary pathway—the kallikrein kininogen system resulting in the release of kinin, a potent vascular permeability factor.

Since activations of all the mentioned mediators associated with the increased vascular permeability can theoretically be initiated by a common factor so called Immune Complex, various means of searching for the presence of such factor

*Department of Pediatrics, Faculty of Medicine, Chulalongkorn Hospital, Chulalongkorn University

has recently been scrutinized. There are two indirect evidence supporting this view. Firstly, gammaglobulins (Ig G, Ig M) and complement (C₃) suggesting immune complex were demonstrated in the glomerular structure of the kidney tissue biopsied from the serologically proved patients infecting with dengue virus⁽⁷⁾. Secondly, viral antigen, complement (C₃) and gammaglobulin were also detected on the surface of circulating granulocytes of these similar patients by mean of direct immunofluorescent technique⁽⁹⁾. Such bits of informed evidence although admittedly preliminary, and as yet inconclusive would serve as a stimulant to the further confirmation at depth of the triggering mechanism in the pathogenesis of increased vascular permeability associated with dengue - virus - infected patients.

In accordant with the bleeding concerned, internal hemorrhage has always been a specially accelerating issue to all. Accepting that the mechanism of such bleeding is rather of complexity, and that the available information is far from completeness, two factors as speculated await confirmation. First: the factor (s) enables to interfere with the local protective mechanism of the gastrointestinal mucosa and it renders to hemorrhagic phenomena, namely aspirin and its neighboring compounds, and spices. Second: the systemic effect of circulatory disturbance of which, had its process not been interrupted would lead into micro-circulatory failure, then induce tissue ischaemia and eventually bleeding diathesis ensue. Evidence of intravascular clotting, in addition to that has already been mentioned, also appears to be real but it is not so prominent as one would expect. Thus the prospect of therapeutic interven-

tion with anticoagulant drug such as heparin is not enthusiastically participated at this very moment.

Reference

1. Tuchinda, P.: Clinical Review on Dengue Hemorrhagic Fever of Thailand. Delivered at Postgraduate Lecture Course. Siriraj Hospital, Mahidol University, August 18, 1972.
2. Nisalak, A., et al.: Observations Related to Pathogenesis of Dengue Hemorrhagic Fever. III Virologic Studies of Fatal Disease. Yale J. Biol. Med. 42: 293, 1970.
3. Varavithaya, C., et al.: Thai Hemorrhagic Fever. Chulalongkorn Med. J. 14: 217, 1969.
4. Nimmannitya, S., et al.: Dengue and Chikungunya Virus Infection in Man in Thailand, (1963-1964). I. Observations on Hospitalized Patients with Hemorrhagic Fever. Amer. J. Trop. Med. Hyg. 18: 954, 1969.
5. Russell, P.K., et al.: Anti-Dengue Immunoglobulins and Serum Beta Ic Globulin Levels in Dengue Shock Syndrome. J. Immunol, 102: 412, 1969,
6. Phanichyakarn, P., et al.: Serial Serum Beta Ic Globulin Determinations in Individuals with Dengue Hemorrhagic Fever. Asian J. Med. 8: 373, 1972.
7. Futrakul, P, etal : Studies on Renal Function and Reticuloendothelial - System Clearance in Thai Children with Dengue Hemorrhagic Fever. J. Med. Ass. Thailand (In Press).
8. Mitrakul, C., et al.: Hematological Aspect in Dengue Hemorrhagic Fever. Delivered at Post - graduate Lecture Course. Chulalongkorn Hospital. Oct. 26, 1972.
9. Bhamarapravati, N., et al.: Personal Communication.