Review of: "Etiology Models of Antibody Triggered Histamine Intolerance Inducing Kawasaki Disease and Multisystem Inflammatory Syndromes Diseases"

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This article by D. Ricke follows other ones of this author on the same subject. It has the merit of drawing attention on a possible role of histamine, histamine secreting cells (primarily mast cells) and histamine metabolism in Multisystem Inflammatory Sindrome of children (MIS-C) and adults (MIS-A) and in Kawasaki disease.

The hypothesis that histamine contributes to these diseases is based principally on symptoms analogy among these diseases, anaphylaxis and histamine intolerance. It is assumed that histamine intolerance can be driven by antibody dependent release of histamine stores in histamine hypersensitive subjects. Such a massive release is yet unproven, and the same applies to intermediate steps required by the model.

Histamine intolerance is considered in the literature to follow exogenous amine assumption (Comas-Basté et al. Histamine intolerance: The current state of the art. Biomolecules 10: 1181 [26 pages], 2020). Endogenous release occurs in anaphylaxis and a role for intolerance to amines and to other mast cell released factors has not yet been proved in anaphylaxis.

Some similarity among Kawasaki disease, MIS-C, MIS-A, anaphylaxis and histamine intolerance is counterbalanced by differences in clinical features and, as far as up to date, in pathophysiology (Patel P. Clinical characteristics of Multisystem Inflammatory Syndrome in adults. JAMA Netw. Open 4: e2126456 [15 pages], 2021 - Sharma C. et al. Multisystem Inflammatory Syndrome in children and Kawasaki disease: A critical comparison. Nat. Rev. Rheumatol. 17: 731-748, 2021).

Therefore, one should think of a role for antibody dependent histamine release in histamine intolerant subjects as a possible additional pathogenic mechanism, not the single nor a major one, for Kawasaki disease, MIS-C and MIS-A except perhaps in a strict minority of patients.

A key point of this article is therefore to stimulate future studies addressing circulating histamine levels in patients with MIS-A, MIS-C and Kawasaki disease, as well as the other links in the modeled chain of events.