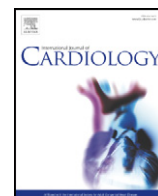




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Letter to the Editor

Serum IgE antibody concentrations and the risk of Kounis syndrome

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It is known that immunoglobulin E (IgE) is an important regulator of allergic reactions because it activates mast cells to release their inflammatory mediators by binding to high affinity FcεRI receptors situated on the mast cell surface. Inflammatory mediators such as histamine, neutral proteases, arachidonic acid products, platelet activating factor and a variety of cytokines and chemokines released during the activation process can induce coronary artery spasm and atheromatous plaque erosion and rupture culminating in the development of Kounis syndrome [1]. In addition to mast cells, other inflammatory cells such as dendritic cells, eosinophils, platelets, monocytes, and macrophages also bear high affinity receptors on their surfaces [2]. Therefore, IgE's targets likely extend beyond mast cells in order to induce coronary events and Kounis syndrome.

In the very interesting analysis published in this journal [3] Dr Ivy Shiue commenting on a national population-based multi-year cross-sectional study conducted by United States National Health and Nutritional Survey 2005–2006 (NHANES), wondered if higher serum IgE antibody concentrations are associated with adult cardiovascular disease. NHANES 2005–2006 collected questionnaire and laboratory data on United States citizens and was also the first nationwide assessment of serum total IgE and specific IgE. This study showed that people with higher total IgE levels were likely to have coronary heart disease and only shrimp serum specific IgE antibody was significantly associated with coronary heart disease. Dr Shiue added that although an association between total serum IgE concentrations, shrimp specific antibody and coronary heart disease was found,

causality cannot be established and suggested future studies with very large study populations.

Similar results have been found in previous studies. In a cross-sectional population study [4] which was carried out on a group of 262 men and 315 women, a statistically significant positive correlation between increased IgE levels in men and previous myocardial infarction, stroke and peripheral arterial disease was found irrespective of total cholesterol and LDL levels. In another study [5] concerning 156 patients with coronary heart disease who were admitted to cardiological wards, total IgE levels were found to be significantly higher in patients with unstable angina and acute myocardial infarction compared to patients with stable angina and controls. In a prospective [6] study of 621 patients followed for about nine years, a significant correlation between the increased IgE levels and the incidence of acute myocardial infarction in males was found. When IgE levels were above 200 kU/L the incidence of non-fatal myocardial infarction was seven times higher. In a recent study [7] of 195 patients suffering from ischemic heart disease serum IgE levels were increased as compared to the control group of healthy individuals. IgE serum levels on the days 1, 7, 14, and 40 after acute myocardial infarction did not revealed any significant changes. Males had significantly higher IgE than females.

However, the questions which arise are: first, increased IgE levels in acute coronary events are the result or precede coronary events. Second, elevated IgE levels are indicative of their participation in the development of the coronary event or are increasing due to inflammatory reaction from tissue damage. There are two studies answering to the above questions. In a prospective study, with initially healthy hyperlipidemic men who suffered myocardial infarction, the levels of IgE as well as of other immunoglobulin classes such as IgA, IgG were significantly higher than the matched healthy controls [8]. The risk of myocardial infarction increased with the increase of immunoglobulin level and was independent of adjustment for confounding factors such as age, smoking, of blood pressure. The authors concluded that myocardial infarction was preceded by immunologic processes involving antigen–antibody systems. In a second study it was found that circulating IgE levels in patients with atherosclerosis associate with plaque instability which precedes acute coronary events [9]. In this study, immunostained parallel frozen sections of human atherosclerotic lesions from shoulder regions of atheromatous plaque showed that IgE and its high-affinity receptor FcεRI colocalize with mast cells and macrophages. It is known that shoulder sites of coronary plaques are susceptible to erosion or rupture which means that IgEs, their receptors and inflammatory cells invade this area before an actual initial coronary event.

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Therefore the observed higher levels of immunoglobulin E in patients with cardiovascular diseases and their association with ischemic heart disease should serve as an early marker of atherogenesis which could predict future coronary events and Kounis syndrome.

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The authors of this manuscript have certified that they comply with the Principles of Ethical Publishing in the International Journal of Cardiology.

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