Venue: PYRAMID 2
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1030-1145 hr

Symposium 3A: Inflammatory markers

S3A-1. Inflammatory markers and cardiovascular diseases – bystanders or culprits?

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Chronic inflammation is a major feature of the atherosclerotic process that underlies most forms of cardiovascular disease (CVD). The measurement of circulating inflammatory markers such as high sensitivity C-reactive protein (hs-CRP) has been acclaimed as a means of providing diagnostic information which is independent of the classical CVD risk factors. This presentation will review the proposition that circulating inflammatory markers provide additional tools for the prediction of the risk of future CVD events. In order to examine this proposition, it is necessary to refine the hypotheses that underlie the association between inflammation and CVD. Does an increased level of a circulating marker reflect the presence or absence of culprit lesions in large and medium arteries or does it reflect a systemic milieu that encourages the progression of atherosclerosis in general? It could be argued that central adipose tissue may constitute the major source of circulating inflammatory markers, implying that elevated levels are merely a surrogate for obesity and insulin resistance. Underlying hypotheses has important implications for the interpretation of elevated levels of inflammatory markers because these could arise from a wide range of potentially confounding causes. The main strength of this group of tests is their sensitivity rather than their specificity. As such, they are more likely to be useful for the exclusion of CVD. Unfortunately, this point has not been appreciated in the clinical arena. The demand for tests that assist the positive diagnosis of future CVD risk has driven a search for inflammatory markers that are more specific for CVD. Despite claims and counterclaims, it is difficult to discern any clear solution to this problem. Alternative approaches such as multiple analytes on proteomics platforms may be required to fulfil diagnostic requirements.

S3A-2. Clara cell 10 kDa protein as an anti-inflammatory marker

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Clara cell 10-kDa protein (CC10), also called as protein 1(P1), is a non-glycoprotein which is the predominant product of Clara cells, a nonciliated cell population in the epithelial lining of bronchioles in the lung. The author isolated the protein from pathologic urine and thus prepared recombinant P1 and monoclonal antibodies with well-defined epitopes. In the ELISA serum concentration is 0.5-6.0 mg/L in normal individuals and decreased in smokers. Recombinant P1 was shown to bind with phospholipase A2 (PLA2) and PI-specific phospholipase C (PI-PLC), and inhibit their activities. Serum and BALF CC10 concentrations in asthmatic nonsmokers were significantly lower than in healthy non-smokers. The longer the duration, the lower the value is. Vicious cycle might be formed to give the disease down hill course. Knockout mouse experiments showed aggregation of allergic and inflammatory reaction, giving similar clinical feature with IgA nephropathy. SNPs were thus investigated by alleic PCR to show that adenine allele accumulation in G34A is associated with IgA nephropathy and sarcoidosis and reflects the disease prognosis. By a reporter assay the production is partly influenced by some transcriptional factors induced by -interferon. P1/CC10 is one of immunomodulatory /antiinflammatory components involving down-regulation of inflammatory reaction in epithelium evoked by direct exposure to environment.

S3A-3. Inflammatory markers and cancers

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Patients with cancers often present with inflammatory symptoms and laboratory data which have been shown to be mediated by proinflammatory cytokines produced by the cancer cells themselves. The inflammatory symptoms include fever, night sweating, weight loss, and general malaise that may be attributable to the cancers producing IL-1 and TNF- . The inflammatory laboratory findings include high C-reactive protein (CRP) level (attributable to IL-6, IL-11 produced by cancers), neutrophila (G-CSF, GM-CSF, M-CSF), eosinophilia (GM-CSF, IL-5), thrombocytosis (IL-6, GM-CSF, thrombopoietin), anemia (IL-1 and hepcidin upregulated by IL-6), disseminated intravascular coagulapathy (DIC/pre DIC (IL-1 and TNF- , that enhance the expression of endothelial plasminogen activator inhibitor and tissue thromboplastin), hemophagocytic syndrome (IFN- , especially in malignant lymphoma), and hypercalcemia (parathormone-related protein: PTH-rP). We shall present the following data: (1) Patients with malignant tumors producing colony-stimulating factor (CSF) are characterized by fever, high CRP, liver dysfunction in addition to marked neutrophilic leukocytosis. (2) Patients with thrombopoietin-producing cancers are associated with thrombocytosis. (3) Patients with malignant tumors producing IL-8 only present with marked neutrophilic leukocytosis. (4) Production of chemokines by malignant tumors such as Hodgkin's lymphoma involves in formation of their pathohistological features associated with infiltration of T cells, eosinophils, macrophages, NK cells and basophils. Through the presentation of these data we clearly show that the production of proinflammatory cytokines by human carcinomas contributes to the inflammatory symptoms and laboratory data in these patients.