EVALUATION OF SERUM LEVELS OF CRP&IL-6 IN CORONARY ARTERY ECTASIA

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EVALUATION OF SERUM LEVELS OF C-reactive protein (CRP) and Interleukin-6(IL-6) IN CORONARY ARTERY ECTASIA

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Objective: Coronary artery ectasia (CAE) is an uncommon angiographic finding and uncommon manifestation of atherosclerosis defined as an arterial segment with a diameter of at least 1.5 times the diameter of the adjacent normal coronary artery. The exact mechanism of its development is unknown; Study was done in an attempt to find an inflammatory etiology in coronary artery ectasia, by measured the serum levels of hs CRP & IL – 6 and correlated to the presence or absence of CAE.

Method and results: This study evaluated plasma hs C-reactive protein (CRP) and interleukin-6 (IL-6) levels, as specific markers of inflammation, in 15 patients with coronary artery ectasia (CAE) without stenosis,15 patients with CAE with stenosis and 30 patients with obstructive coronary artery disease without ectasia compared the results with those 15 subjects with angiographically normal coronary arteries. The mean hs CRP levels among the studied groups was 1.1 ± 0.74 ng/dl, 1.2±1.5 ng/dl, 1.5±2.4 ng/dl , 0.33±0.23 ng/dl in group A, B, C and D respectively. The mean IL-6 levels among the studied groups were 5±1.8 pg/dl,4.6±3.55 pg/dl, 4.9±3.7 pg/dl, 2.6±0.61 pg/dl in group A, B, C and D respectively. In comparison of each group with control there is significant P-value,

Serum hs CRP and IL-6 levels were found to be significantly higher ($P < 0.001, 0.03, 0.01$), and ($P < 0.0001, 0.04, 0.02$) respectively in patients with CAE suggesting that inflammations may be involved in the pathogenesis of CAE. IL-6 levels were 3.3 ± 0.7 pg/dl in patients with one vessel. Lesion, 4.2 ± 1.1 pg/dl in patients with 2 vessels lesion and 6.3 ± 3.8 pg/dl in patients with 3 vessels lesion. ($P < 0.02$).

Conclusions: - Inflammation plays a major role in the aetiology of CAE as well as coronary artery stenosis. IL-6 and hs CRP as inflammatory markers were elevated in patients with CAE and also were elevated in patients with coronary artery stenosis. IL-6 level was related to the severity of the disease as it was elevated in patients with more vessels affection than in patients with one vessel affection so it could be monitored and used as a severity marker.

Keywords☹ C-reactive protein-interleukin- coronary- ectasia- inflammation- coronary artery disease.)

List of Abbreviations

- **CAE:** Coronary artery ectasia**.**
- **hs CRP:** High sensitive C-reactive protein
- **IL-6:** interleukein-6
- **LAD:** Left anterior descending coronary artery
- **LCX:** Left circumflex coronary artery
- **RCA:** Right coronary artery.
- **LAO:**Left anterior oblique .
- **RAO:**Right anterior oblique .
- **MMPs:** Matrix metalloproteinases.
- **TIMPs:** Tissue inhibitors of MMPs .
- **LDL:**Low density lipoproteins.
- **HDL:**High density lipoproteins.
- **FH:** Familal hyperdyslipedemia.
- **AAA:** Ascending aortic aneurysm.
- **IMT:** Intimal medial thickness.
- **VEGF:** Vascular endothelial growth factor.
- **ICAM:** Intra cellular adhesive molecules.
- **VCAM:** Vascular cellular adhesive molecules.
- **CAD:** Coronary artery disease.
- **OCAD:** Obstructive coronary artery disease.
- **NO:** Nitric oxide.
- **HLA:** Human leucocytes antigen.
- **TIMI:** Thrombolysis in Myocardial Infarction.
- **CFR:** Coronary flow reserve.
- **MPV:** Mean platelet volume.
- **IVGG:** Intra venous gamma globulin.
- **SPECT:** Spaital positron emission computerized tomography.
- **KD:** Kawasaki disease.
- **ET-1:** Endothilin-1.
- **ROS:** Reactive oxygen species.
- **MCP:** Monocytes chemo attractant protein.
- **SMC:** Smooth muscle cells.

- **M-CSF:** Macrophage colony simulating factor.
- **TNF:** Tumor necrotizing factor.

- **VLDL:** Very low density lipoprotein.
- **AII:** Angiotensin II.
- **AGE:** Advanced glycated end products.
- **SAA:** Serum amyloid A.
- **INF:** Interferon.
- **Th1:**T.helper cell 1
- **MI:** Myocardial infarction.
- **TG:** Triglycerides.
- **IHD** Ischemic heart disease.
- **ACC:** American college of cardiology.
- **AHA:** American heart association.
- **DM:** Diabetes mellitus.
- **SF**: Slow flow

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Introduction

- Coronary artery disease is the most common form of heart disease and the most important single cause of death world wide.[1]

- Coronary artery ectasia (CAE) is an uncommon angiographic finding and defined as an arterial segment with a diameter of at least 1.5 times the diameter of the adjacent normal coronary artery. [2, 3]

- The prevalence of CAE in the literatures varies between 1.2–6%.[4 ,5 ,6]

- Angina pectoris is a frequent presentation of the disease.[7]

- CAE was suggested to be a variant of obstructive coronary artery disease and is considered an accompaniment or a variant of coronary atherosclerosis.[4, 8]

- It is sometimes associated with more extensive coronary stenosis, suggesting that ectasia and stenosis my have pathophysiological mechanisms in common. [9, 10]
In fact thinning of vascular media has been associated with advanced atherosclerosis.[11]Moreover, recent advances in basic science have established a fundamental role for inflammation in mediating all stages of atherosclerosis starting from initiation through progression and ultimately the thrombotic complications. [12]

- C-reactive protein (CRP) is a protein produced by hepatocytes and released into blood stream any time there is active inflammation in the body. It is among the most sensitive markers of systemic inflammation.[13]

- Proinflammatory cytokines have been shown to play a role in atherogenesis and the development of acute coronary syndrome among which is interleukein-6(IL-6) which originates from T-helper cells and macrophages and promotes B-cell growth and antibody production.[14]

Aim of the work

In an attempt to find an inflammatory etiology in coronary artery ectasia, the serum levels of hsCRP & IL – 6 in patients with stable coronary artery disease were measured and correlated to the presence or absence of coronary artery ectasia.

Anatomy of coronary arteries

There are three main coronary arteries that supply the heart:

a) The left anterior descending coronary artery (LAD) which supplies the anterior two thirds (2/3) of the ventricular septum and part of left ventricular wall.

b) The left circumflex coronary artery (LCX) which supplies the lateral wall of the left ventricle, in some cases the circumflex artery also supplies the inferior portion of the left ventricle.

c) The right coronary artery (RCA) which supplies the inferior portion of the heart and posterior one third (1/3) of the ventricular septum.[15]

- Both the LAD and LCX are branches from left main coronary artery. The term "dominance" often is used to describe coronary artery anatomy; the dominant vessel is the one that supplies the posterior diaphragmatic Portion of the interventricular septum and the diaphragmatic surface of the left ventricle. The RCA is dominant in about 85% of humans. [16]

Left coronary artery:

The left main coronary artery arises from the upper portion of the left aortic sinus. Then emerges from behind the pulmonary trunk within a short distance (2 to 10 mm) then usually bifurcates into LAD and LCX.[16]

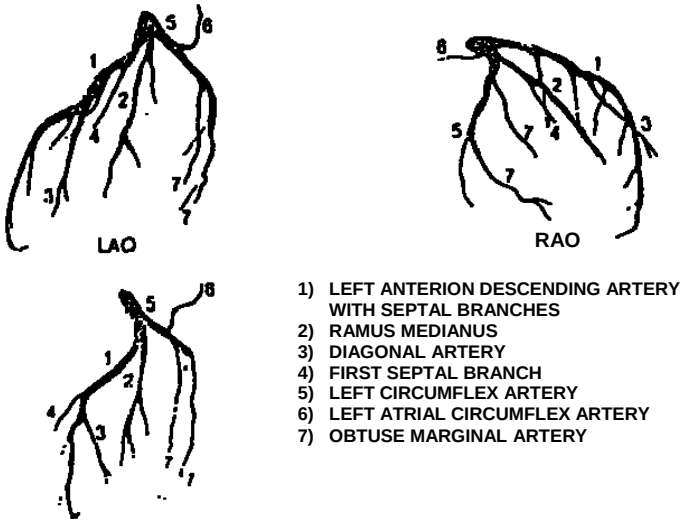
- Left anterior descending coronary (LAD):

The LAD passes down the anterior interventricular groove toward the cardiac apex. Its major branches are septal and diagonal branches. The septal branches pass into the interventricular septum and interconnect with similar septal branches passing upward from the posterior descending branch of RCA to produce a network of potential collateral channels. The diagonal branches of LAD pass over the anterolateral aspect of the heart; more than 90% have one to three branches. [17]

- In 37 percent of patients, the left main coronary artery trifurcates into LAD, LCX and ramus intermedius. In these cases the ramus arises between the LAD and LCX arteries and usually supplies the free wall along the lateral aspect of the left ventricle**.** [16]

- The LAD courses beyond the left ventricular apex and terminates along the diaphragmatic aspect of the left ventricle in 78 percent of patients. The LAD fails to reach the diaphragmatic surface and terminates at or before the apex in 22 percent of patients.[18]

LEFT CORONARY ARTERY



LAO-cranial angulations

Fig.(1): Anatomy of left coronary artery.[19]

Left Circumflex artery (LCX):

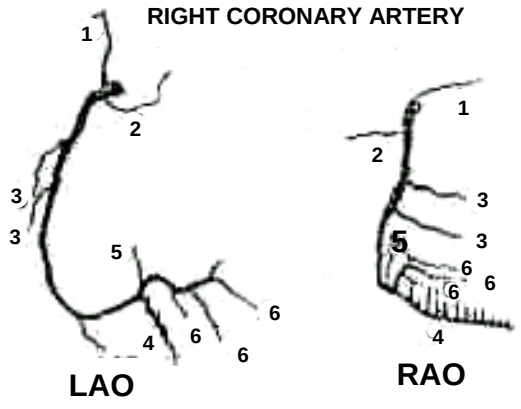
The circumflex artery originates at bifurcation of left main coronary artery and passes along the left atrioventricular groove. The left circumflex artery usually gives off one to three large obtuse marginal branches, as it passes down the atrioventricular groove. The branches of the left circumflex coronary artery are variable; but may include the sinus node artery, the left atrial circumflex branch, the anterolateral marginal branch, the distal circumflex branch, one or more posterolateral marginals and the posterior descending artery. The anterolateral marginal is directed along the anterolateral wall toward the apex. [17]

Right coronary artery (RCA):-

The right coronary artery originates from the right aortic sinus at a point somewhat lower than the origin of the left coronary which originate from the left aortic sinus. It descends in the right artioventricular groove running posteriorly at the acute margin of the right ventricle toward the crux (a point on the diaphragmatic surface of the heart where the right atrioventricular groove, the left atrioventricular groove and the posterior interventricular groove come together). The first branch of the right coronary artery is considered to be the conal artery. Its primary importance is to serve as a source of collateral circulation in patients with left anterior descending coronary artery occlusion. In 50% of the hearts, the conal artery is not actually a branch of the right coronary artery, but arises from a small, separate ostium in the right aortic sinus just above the right coronary ostium. [17]

- The second branch of the RCA usually is the nodal artery, it was found that this vessel originated from the RCA in 59%, from the LCX in 38% and had a dual supply in the remaining 3%**.** [20]

- The midportion of the RCA usually gives rise to one or several medium sized acute marginal branches. These branches supply the anterior wall of the right ventricle. The next important branch of the RCA is the posterior descending artery.



1) CONUS ARTERY
2) S.A NODE ARTERY
3) ACULE MARGINAL ARTERY
4) POSTERIOR DESCENDING ARTERY WITH SEPTAL BRANCHES
5) A.V NODE ARTERY
6) POSTERIOR LEFT VENTRICULA ARTERY

Fig. (2): Anatomy of right coronary artery [19]

Histology of the normal Coronary artery

The basic organization of the coronary arterial wall is similar to all arteries in that three concentric layer can be distinguished:

- An inner most (luminal) layer, the intima (tunica intima).

- A middle layer, the media, and

-An outermost (external) layer, the adventitia.

The Intima:

The intimal layer consists of the following:

- A lining layer of endothelial cells; which are oriented longitudinally relative to the artery and are attached by occluding junctions and gap (communicating) junctions. - The endothelium provides a smooth luminal lining and a selective diffusion barrier between the blood and the other wall layer. Now it is known that endothelial cell have a number of metabolic and endocrine functions that play a critical role both normally and in various disease states.Subendothelial layer containing connective tissues and smooth muscle cell.

- The internal elastic membrane (internal elastic lamina, elastica interna); which separate the intimal layer from the media layer. It is a fenestrated sheet of elastic tissue, and may be fragmented, duplicated or focally lost with advancing age or intimal disease. [21]

The Media:

- The media consists of multiple layers of smooth muscle cells and connective tissue (elastic fibers, collagen, and proteoglycans). The amount of elastic tissues is less and the number of smooth muscle cells greater in the epicardial coronary arteries compared with other elastic vessels.[22] The media consists of up to 40 layers of circumferentially or helically oriented smooth muscles, the normal media ranges in thicknes from 125 to350 um, average 200 um.[21]