Review Article

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hsCRP, A Risk Factor Behind Atherosclerosis

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Abstract

Novel risk factors are emerging behind the genesis of atherosclerosis in today's era of moleculogy. High sensitive CRP is one of the frontiers in this field besides homocysteine, fibrinogen and Lp (a). We report a case of premenopausal lady without conventional risk factors with malignant manifestations of atherosclerosis having only elevated hsCRP to explain the scenario. Being a biomarker behind inflammatory vascular stress, it stands out a promising molecule in today's atherobiology. Exercise and statins can bring down this inflammatory insult, resulting in a healthy vascular tree.

Keywords: hsCRP; Atherobiology; Atherosclerosis; LMCA; ECG.; Novel; Atherosclerosis; Cardiovascular.

Introduction

We report a case of 39 year old premenopausal lady presenting to the Cardiology OPD of AIIMS, Bhubaneswar with effort dyspnea NYHA class III with rest angina, dysphagia and dull abdominal pain. She was thin built (36kg),nondiabetic and nonhypertensive. She denied any history of familial coronary artery disease. Physical examination was unremarkable except presence of mild cardiomegaly with presence of LVS_4. ECG revealed old anterior wall myocardial infarction with ST elevation in aVR more than V_1 suggestive of LMCA lesion as depicted below. Serum chemistries including blood glucose, lipid panel, renal profile were within normal limit.

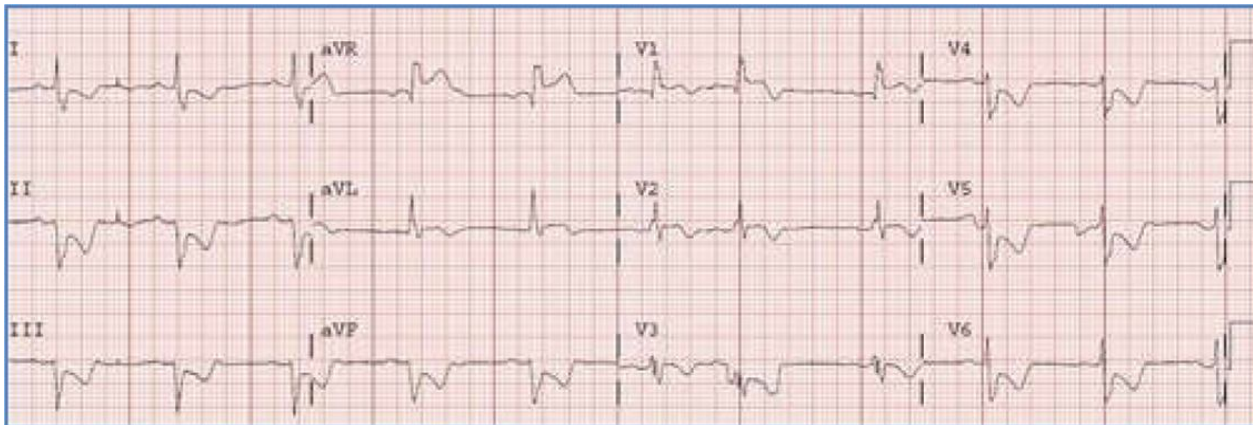

Fig. 1: ECG showing LMCA occlusion

We carried out further biomarker analysis including hsCRP, plasma fibrinogen, serum homocysteine and Lp (a) which were as follows: ***3.9 mg/L***, 130mg/dl, 10 µmol/L and 10 mg/dl respectively. Cardiac Troponin I was negative and NT PRO BNP was elevated modestly i.e. 550 pg/ml.

Chest roentgenogram revealed cardiomegaly with aneurysmal dilation of aortic arch with wall calcification. Echocardiography revealed dilated left ventricle with RWMA in LAD territory with severe LV systolic dysfunction with hugely dilated descending aorta in PLAX view. Aortic arch interrogation in suprasternal echo window revealed a thin retrograde dissection flap freely hanging in the arch with a very small and short false lumen. We ruled out cardiovascular syphilis by doing VDRL in view of giant arch aneurysm.

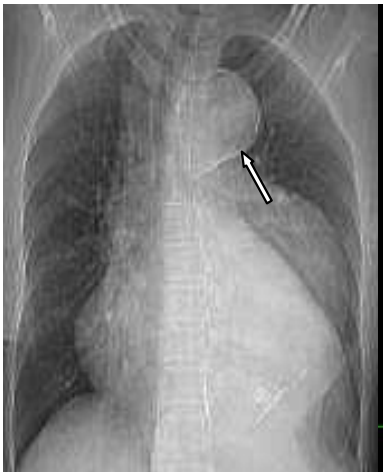

Fig. 2: X-ray showing cardiomegaly with aneurymal arch

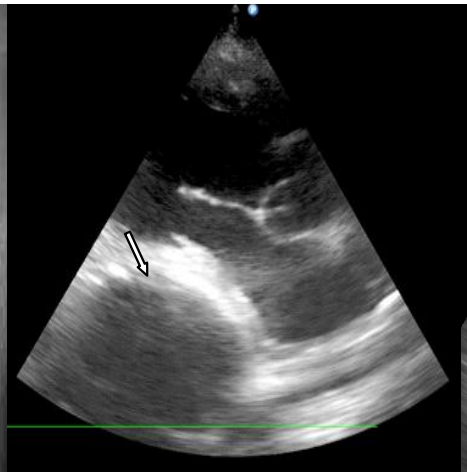

Fig. 3: Echocardiography showing hugely dilated aorta in PLAX view

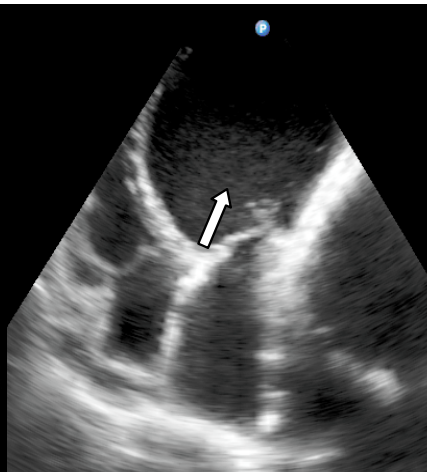

Fig. 4: Hugely dilated LV in A_4CH view

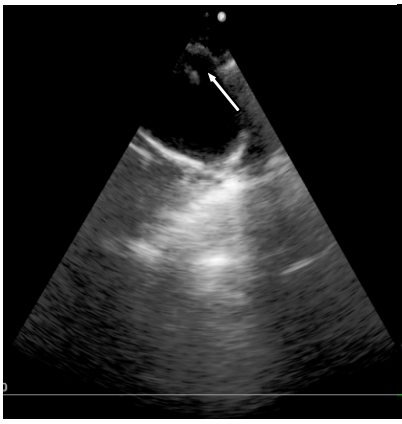

Fig. 5: Echocardiography showing small false lumen

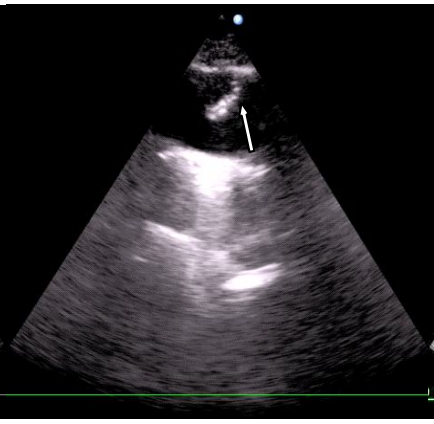

Fig. 6: Thin hanging dissection flap

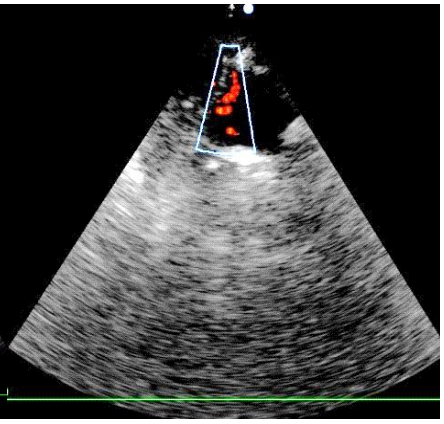

Fig. 7: Retrograde flow in false lumen

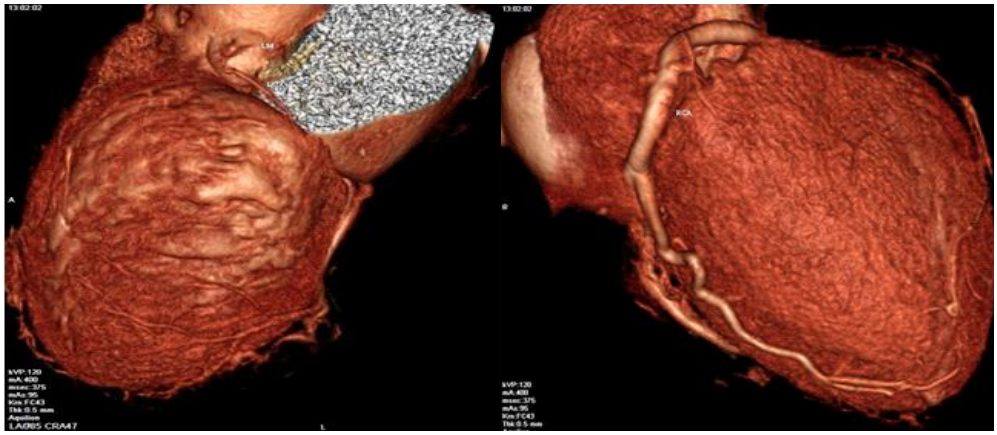

Fig. 8: CT CAG revealing near total occlusion of LMCA with thinned out and diseased LCX with distal LAD being filled by collaterals

Fig. 9: A normal RCA

Fig. 10: CT Aortic angiogram revealing aortic arch and descending aorta aneurysm

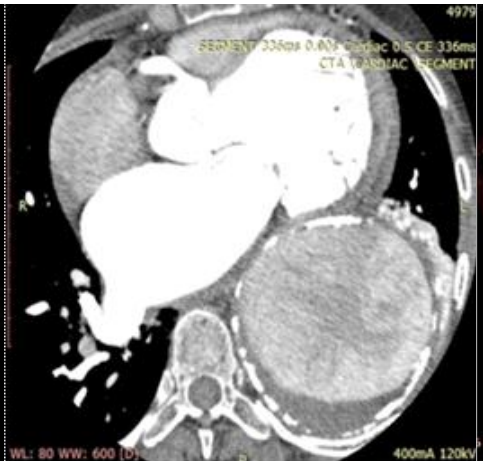

Fig. 11: Intraluminal thrombus with calcification in arch aneurysm

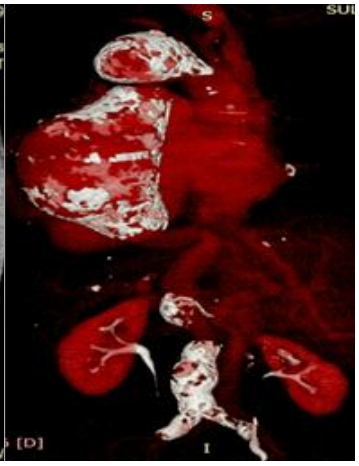

Fig. 12: Infrarenal and suprarenal aortic aneurysm with left renal artery stenosis with renal atrophy

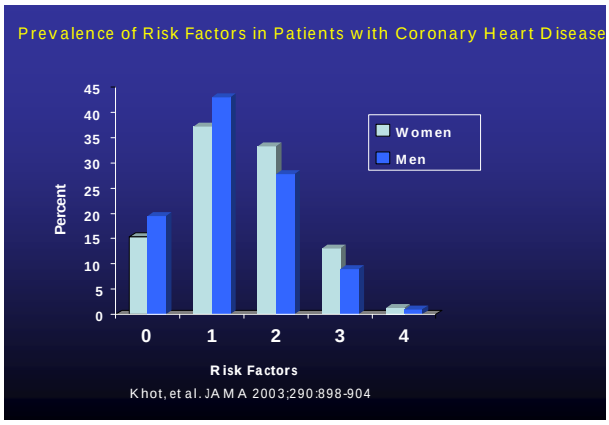

Fig. 13: CHD and no conventional risk factors

Coronary CT angiography revealed near total occlusion of LMCA with trickled flow into thinned out and diseased LCX with no flow in proximal LAD and distal LAD partly being filled by growing collaterals from normal RCA.

We performed CT angiography of thoracic and abdominal aorta to delineate the extent of vascular atherosclerosis as Carotid Doppler revealed minimal atherosclerotic changes without significant obstruction. Aortic angiogram revealed huge aortic arch and descending aorta aneurysm with intraluminal thrombus and wall calcification with aneurysmal involvement of suprarenal and infrarenal aorta with significant left renal artery stenosis and left renal atrophy. The aforesaid patient revealed atherosclerosis in most malignant form in form of significant coronary artery disease with LMCA lesion with significant LV systolic dysfunction, aortic arch aneurysm with intraluminal thrombus and wall calcification with a thin hanging retrograde dissection flap, infra and suprarenal aortic aneurysm with left renal artery stenosis with atrophic left kidney. We advised the patient to undergo immediate CABG with surgical resection of arch aneurysm with graft repair. Although endovascular aneurysm repair (EVAR) was an immediate option, as the patient was ideal candidate for CABG, we opted for surgical correction of aneurysm besides CABG. We did not think for left renal artery stenting as DTPA renogram did not dictate about the benefit of renal intervention in non functioning left kidney. Post procedure patient was on ant ischemic and antiplatelets and was uneventful. Patient's dyspnea now has abated to moderate extent and doing fare now. We were amazed to see such a malignant and myriad manifestation of atherosclerosis where conventional risk factors were absent and out of the novel risk factors only hsCRP was elevated to a higher level of 3 mg/L. Although recent literature clearly describes hs CRP as a novel risk factor, our case was a golden witness to this hypothesis. Although hsCRP is not a mandatory routine in screening atherosclerosis, our case dictates not to forget to do an hsCRP before leaving a patient with atherosclerotic cardiovascular disease. Only exercise and statin as evidenced in JUPITER trial can bring down this hsCRP, we can say no to these malignant manifestations of atherosclerosis by using these two simple weapons.

Discussion

Despite the popular myth that only about 50% of patients with CHD have traditional risk factors, the data from Khot and colleagues which looked at risk factor prevalence in 122,458 patients enrolled in 14 major clinical trials of CHD during the prior decade revealed that relatively few had more than two risk

factors, *only about 15% of women and 20% of men had no traditional risk factors.* Nonetheless, given the likelihood that non-traditional risk factors may play a significant role in cardiovascular disease,modern atherobiology identified four major risk factors i.e. hsCRP, fibrinogen, homocysteine and Lp(a) which opened doors to both risk prediction and therapeutic option. MRFIT trial [1] was one of the earliest study to delineate the role of hsCRP behind genesis of cardiovascular disease, subsequently it was included in *Reynolds risk score* [2] as one of the cardiovascular risk factor in defining population at risk. hs CRP otherwise known as *poor man's risk factor* [3] explains the scenario when a village farmer lands in large myocardial infarction without any prior harbor of conventional risk factors and it is only vascular inflammation that ignites the vascular milieu to have florid atherosclerosis [4]. Our case was unique as this woman in premenopausal age without conventional risk factors had only hsCRP elevated to a higher level to explain this myriad manifestation of atherosclerosis. hsCRP plays a vital role behind genesis of atherosclerosis in Indian population [5,6]. ACC/AHA recommends hsCRP screening as Class IIa recommendation for primary prevention in intermediate risk patients (10-20% 10-year CHD risk) to help direct further evaluation, treatment and in patients with stable CAD or ACS, as an independent marker of recurrent events, including death, MI and restenosis following PCI [7]. If level > 10 mg/L, test should be repeated and patient examined for sources of infection or inflammation. ACC/AHA classify risk as follows:

Low	:	< 1 mg/L
Average	:	1.0 – 3.0 mg/L
High	:	> 3.0 mg/L

Our case is a standing appraisal of the established role of hsCRP behind genesis of atherosclerosis and its penopoly of complications. In our patient hsCRP was elevated i.e 3.9 mg/L which falls in high risk category. Patient was advised high dose atrovastatin 80mg to address the nonaddressed vascular tree with regular morning walk for 30 minutes a day with yogic therapy. Studies are underway to know the cause behind this vascular inflammation, may be the real life stress a contributing factor. hsCRP in today's era stands out as a promising cardiovascular risk factor [8, 9,10], well taken care by exercise and statins.

Conclusion

Our case is an unique witness to the fact that hsCRP is a promising novel risk factor behind CAD. The aforesaid patient had the most malignant manifestations of atherosclerosis in form of giant atherosclerotic aortic aneurysm with dissection and intraluminal thrombus, severe CAD, atherosclerotic renal artery stenosis with renal atrophy, only explained by raised hsCRP level. Taking care of this novel risk factor will bring out a new era in the therapeutic horizon of atherosclerosis.

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