C1 esterase inhibitor deficiency – A rare cause of coronary artery thrombosis

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Abstract

C1 esterase inhibitor (C1-INH) is a serine protease inhibitor that acts on a number of proteins that play a role in the complement, coagulation and kinin-kallikrein cascades. By adhering to specific factors (C1, Factor XIIa, MASP-1, MASP-2, Kallikrein), it helps maintain a balance between thrombin generation and fibrinolysis.

Deficient patients however exhibit an elevated thrombotic risk in response to unregulated complement activation and fibrin formation.

A case of acute myocardial infarction secondary to acute coronary thrombosis as a result of C1-INH deficiency is reported here. With otherwise no evidence of coronary artery disease on angiography, a right coronary artery filling defect was consistent with acute thrombosis rather than rupture of an atherosclerotic plaque. As no other explanation was present for this event, C1-INH deficiency is the likely cause.

Case report

This case review describes the history of a middle aged gentleman, known to have familial **C1-INH** deficiency, suffering an acute coronary artery thrombosis, complicated with deep vein thrombosis (DVT). The diagnosis of familial C1-INH deficiency was made in his teenage years after presenting to hospital with recurrent episodes of urticaria, abdominal pain and angioneurotic oedema which were resistant to treatment with both anti-histamines and parenteral steroids. Tests were consistent with a quantitative deficiency of C1-INH, classical of type 1 hereditary angioedema.

The patient then presented to the emergency department at the age of thirty complaining of a fifteen minute episode of severe central compressive chest pain at rest This was associated with diaphoresis and vomiting. An acute coronary syndrome (ACS) event had to be excluded. Electrocardiogram and echocardiography did not show any features suggestive of a myocardial infarction. However a high **troponin I of 0.4ng/mL** rising to **3.6ng/mL** five hours from symptom onset prompted the caring physician to treat as an non-ST segment elevation myocardial infarction (NSTEMI) with Clopidogrel, intravenous heparin and nitrates. Aspirin was omitted because of a known augmented risk of aspirin-related angioedema in individuals with C1-INH deficiency.. An urgent inpatient coronary angiography was performed by the cardiologists. This revealed a right coronary artery filling defect in the middle segment, consistent with intracoronary thrombosis rather than rupture of an atherosclerotic plaque **(Figure 1).** His stay at coronary care unit was complicated with DVT of the right and left lower limb, despite adequate anticoagulation with intravenous heparin.

He was started on long term warfarin as prophylaxis for future thrombotic events. To date, he remains well without any further coronary arterial or venous thrombotic events. A repeat ECHO, six months after this event, showed normal left ventricular function and good ejection fraction. He still requires high doses of parenteral C1-INH at least twice a month.

Discussion

C1-INH deficiency, contributing towards a pro-thrombotic state as a result of complement over-activation. **(Figure 2.)**

In C1-INH deficiency, over-activation of the complement pathways in turn attenuates cardiovascular risk. The benefits of C1-INH as an experimental therapeutic agent has also helped demonstrate its role in reducing the extent of myocardial ischaemia, possibly by direct influence on neutrophil-mediated ischaemia-reperfusion injury.[9]

In patients undergoing eversion carotid endarterectomy, low levels of C1-INH in patients with an intact lectin pathway seemed to predict earlier re-stenosis as they are unable to regulate complement activation, suggesting that C1-INH has an important role to play in atherosclerosis.[1,6]

Conclusion

We hypothesize that uncontrolled complement activation with insufficient regulation of the lectin pathway (resulting in higher levels of factor XIIa, C1a, MASP-1/2 and kallikrein) as a result of C1-INH deficiency, are the main reasons for the elevated thrombotic risk in such patients. Inhibiting all these serine proteases should protect against myocardial infarction and reperfusion injury, primarily by restoring balance between thrombosis and inflammation.

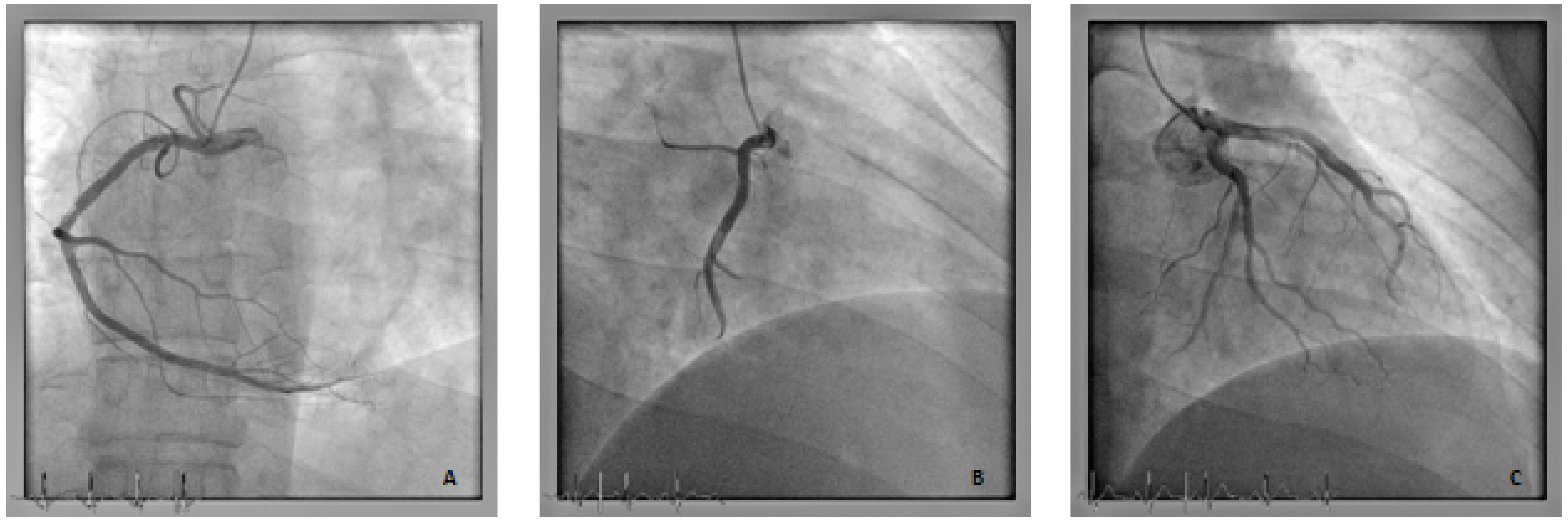

Figure 1.: Inpatient coronary angiogram illustrating a mid-right coronary thrombus (A & B) with a normal left coronary circulation (C).

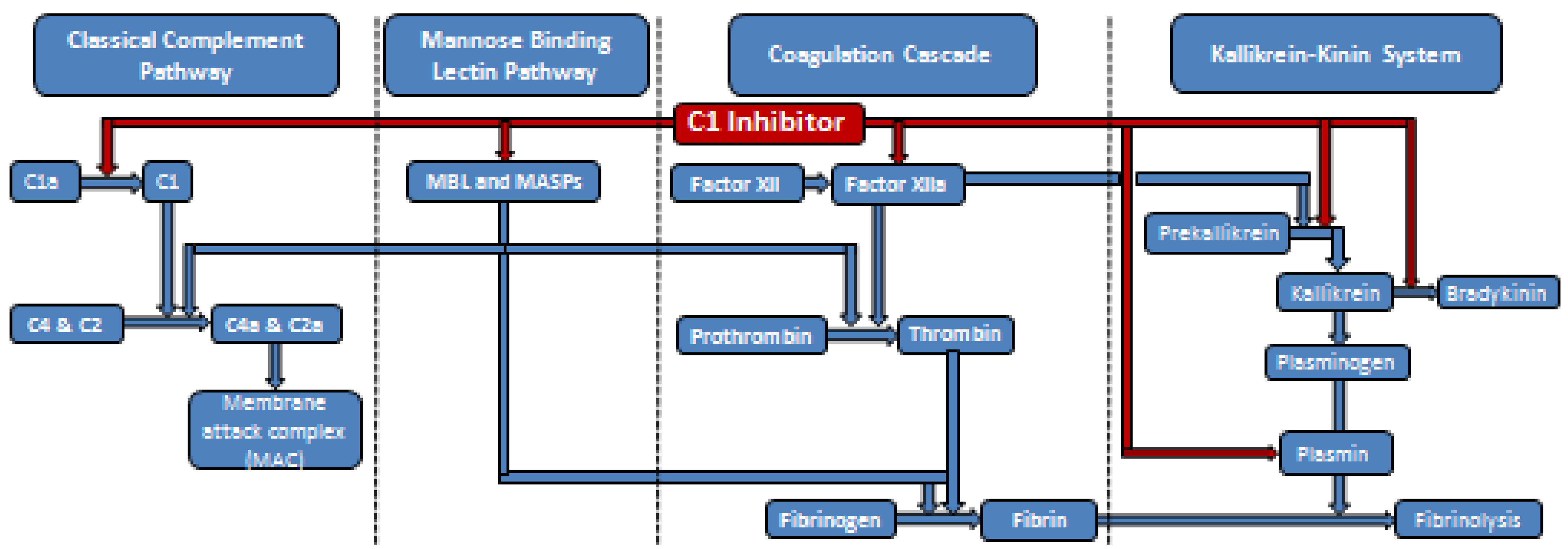

Figure 2, C1 inhibitor's role in the coagulation cascade.

References