Percutaneous Coronary Intervention in a Patient with Congenital Factor XI Deficiency and Acquired Inhibitor

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Key Words
Percutaneous coronary intervention • Factor XI deficiency • Coagulation disorder

Abstract
Background: Factor XI deficiency has been associated with bleeding diathesis mostly secondary to trauma and post-operatively depending on the severity of deficiency. Cases with factor XI deficiency having undergone cardiac surgery and coronary intervention after appropriate replacement therapy have been reported in the past. The presence of inhibitor in factor XI deficiency poses a hematological challenge and literature regarding coronary intervention in such patients is limited. Immunosuppressive therapy, plasma exchange and factor VII product transfusions have been used prior to cardiac interventions in few such reported cases. Method: We report our approach in such a case of Percutaneous Transluminal Coronary Angioplasty in a 72-year-old male of Jewish origin who has congenital factor XI deficiency complicated with acquired inhibitor. Results: In some cases, the acuity of the coronary syndrome may mandate immediate coronary intervention. However, patient’s history of factor XI deficiency and acquired inhibitor pose a major dilemma of further course of action. We performed percutaneous balloon angioplasty in this case with no anti-coagulant and with favorable outcome. Conclusion: Under these circumstances of significant coagulation disorder and based on the case report, we recommend that balloon angioplasty be undertaken with no additional anti-coagulation other than Aspirin.

Background
We report a case of Percutaneous Transluminal Coronary Angioplasty (PTCA) in a 72-year-old male of Jewish origin who has congenital factor XI deficiency complicated with acquired inhibitor. Factor XI deficiency has been associated with bleeding diathesis mostly secondary to trauma and post-operatively depending on the severity of deficiency. Cases with factor XI deficiency having undergone cardiac surgery and intervention have been reported in the past. The presence of inhibitor in factor XI deficiency poses a hematological challenge and literature regarding coronary intervention in such patients is limited.
History

A 72-year-old white male of Jewish origin with history of hypertension and congenital factor XI deficiency was admitted in another institute for symptoms of Unstable Angina (New onset Angina at rest). During that hospital course, patient was noted to have normal physical examination, elevated Troponin I, peak of 259.8 ng/ml (Normal <0.3 ng/ml), prothrombin time/partial thromboplastin time (PT/PTT) of 14.8/78.5 s (baseline). ECG showed normal sinus rhythm, left axis deviation, and left ventricular hypertrophy with minimal ST–T depression in V4–V6. 2D Echo showed minimal concentric left ventricular hypertrophy with normal ejection fraction and wall motion. Patient was discharged with diagnosis of non-ST-elevation myocardial infarction (NSTEMI) on Aspirin 81 mg and Cardizem CD 120 mg.

An outpatient stress echo at our Institute showed 12 mm ST depression in stage 2 of Bruce protocol with anterior and anteroseptal wall hypokinesis. Patient was brought in for cardiac catheterization, which showed right dominant system with calcified left main ostial 30% stenosis, 100% mid left anterior-descending artery (LAD) obstruction, first diagonal (D1) was diffusely diseased, proximal second diagonal (D2) 99% stenosis. Left circumflex proximal 40% and distal obtuse marginal (OM) 99% stenosis (fig. 1a). Right coronary was a small vessel and had mid 50% and ostial posterior descending artery 95% stenosis. Patient’s baseline activated clotting time was 420 seconds (s) and platelet activating unit was 167 U (within normal range).

Patient’s past history was remarkable for pentosuria and lifelong bleeding diathesis. He bled excessively after tonsillectomy at age 10 and after nasal polypectomy at age 13. At age 33 he bled twice post-operatively after a left submandibular gland excision for chronic sialadenitis requiring multiple transfusions of fresh frozen plasma (FFP). In 1965 he was admitted for a left thigh hematoma and his PTT was 79 s. In 1975, he was readmitted for right submandibular gland excision and removal of sebaceous cyst of back; during that hospitalization his PTT was 62.9 s and factor XI level less than 1%. Patient received more than 20 units of FFP. In 1977, he presented with left thigh hematoma, PTT was 54 s, factor XI less than 1%, and with nearly 40 units of FFP the factor XI levels failed to rise, he was diagnosed with factor XI inhibitor and was treated with factor XI/pro-complex concentrate [1]. In 1978, he bled into the left trapezius and was treated with Procomplex, inhibitor level was 90 Bethesda units. In 2002, he had Todd’s paralysis which was associated with infusion of recombinant factor VIIa (rFVIIa) for bruising of left thigh, at that time his factor XI levels less than 1% and the inhibitor was elevated to 26 Bethesda units. His hematological work up from 2000 to 2002 consistently has shown factor XI activity less than 1% and high factor XI inhibitor levels ranging from 17 to 25 Bethesda units, his Lupus anti-coagulant antibody titers were negative. He was recently diagnosed with elevated liver enzymes and hepatitis C likely from the multiple plasma products received.

Patient’s history of factor XI deficiency and acquired inhibitor pose a major dilemma of further course of action in the catheterization lab. A plan to proceed with PTCA without the usage of anti-coagulants was decided in lieu of prolonged PTT at baseline. Initial trial of probing the LAD failed and the risk vs. benefit favored no further intervention in LAD. A decision to do a balloon angioplasty of the diagonal and OM lesions was taken. An XB-4 6 French guide was used and the D2 lesion was reduced from 99% to a residual 40% using Maverick 2 × 12 balloon at 10 atmospheres (atm) for 30 s. The distal OM lesion was reduced to a residual 30% using Quantum 3 × 20 at 10 atm for 30 s (fig. 1b). Procedure was completed with no usage of anti-coagulants. Per-
close device was used for groin closure. Patient was discharged on low dose Aspirin and Cardizem. A repeat stress echo 3 months later showed improvement in anteroseptal wall motion at stress with symptomatic improvement.

Discussion

Factor XI (plasma thromboplastin antecedent, or PTA) is a plasma glycoprotein that participates in the early phase of the blood coagulation and is essential for normal hemostasis [2]. Rosenthal et al. [3] reported hereditary factor XI deficiency in 1953 as a ‘Hemophilia like disease’. The gene coding for this protein has been characterized on the distal long-end of the long-arm of chromosome 4. Congenital factor XI deficiency has been described with autosomal inheritance in homozygous (with severely reduced levels less than 15 U/dl) and heterozygous forms.

A deficiency of factor XI is an unusual coagulopathy in that its bleeding manifestations vary widely depending on the severity of deficiency, ranging from completely asymptomatic course to injury-related bleeding that requires multiple transfusions. However, unlike the hemophilia’s, factor XI deficiency rarely manifests as spontaneous bleeding and is mainly related to injuries [4]. Bleeding can be brisk at the time of injury and can continue for hours and days unless treated. Surgical procedures involving tissues with a high content of plasminogen activators, such as dental extractions, tonsillectomy, urological surgery and nasal surgery are frequently associated with excessive bleeding in factor XI deficient patients irrespective of their genotypes [5].

Biggs et al. [6] suggested that factor XI deficiency might be more frequent among Jews especially of Ashkenazi origin [5]. Sporadic cases have also been reported among Italians, Germans, Japanese, Chinese, Koreans, Indians, American blacks and Arabs [7, 8]. Three Point mutation leading to deficiency have been reported [9].

Traditionally, FFP has been used for replacement therapy in patients with factor XI deficiency, however, such therapy has the risk of volume overload, allergic reactions and potential of transmitting infections. Recently, a factor XI concentrate has been produced which is easy to administer [10]. Recovery of the factor XI with either plasma or concentrate infusion was more than 90% with a mean half-life of 52 ± 22 h [10]. Although effective, factor XI has limitation of being derived from plasma and its thrombogenic potential [11]. rFVIIa is currently being assessed as a possible alternative to plasma derived factor XI replacement. Available case reports suggest that rFVIIa is effective for the treatment of patients with factor XI deficiency undergoing surgery including those with inhibitors [12–14]. The usage of anti-fibrinolytic agents has been considered for procedures where there is local fibrinolysis. Desmopressin has been used in variety of bleeding disorder since the discovery that it raises factor VIIIIC and Von Willebrand factor levels.

Though cardiac interventions and other bypass surgery in patients with factor XI deficiency have been reported [15–17], the development of inhibitor to factor XI in congenital deficient patient poses a significant problem and the literature regarding the management of such patient is limited [18]. Two cases of cardiac intervention in patients with factor XI inhibitor have been reported with successful treatment with immunosuppressive therapy and plasma exchange. Usage of anti-platelet agents after cardiac interventions in such patients may increase the risk of bleeding complications. Peri-procedure usage of Heparin and Glycoprotein IIb–IIIa inhibitors should be avoided in these cases due to elevated ACT at baseline.

However, in some cases, the acuity of the coronary syndrome may mandate immediate intervention, thereby precluding the possibility of a course of Pre-PTCA Immunotherapy or Plasma exchange. Under these circumstances and based on the case report, we recommend that balloon angioplasty be undertaken with no additional anti-coagulation (i.e., no Heparin, no low molecular weight Heparin, no Bivalirudin, no Glycoprotein IIb–IIIa inhibitors), other than Aspirin. If stenting cannot be avoided, consideration should be given to using a heparin or PC coated stent with post-procedure aspirin only (i.e., no Clopidogrel). If Clopidogrel is felt to be necessary (e.g., long stent, imperfect result), a short course of 2 weeks of Clopidogrel would be reasonable with Aspirin at a reduced dose of 81 mg/day. After 2 weeks, the risk for stent thrombosis probably diminishes to such an extent that the patient could be managed with Aspirin alone thereafter.

Conclusion

Factor XI deficiency is a coagulation disorder characterized by bleeding association with trauma and depends on severity of deficiency. It is often seen in people of Jewish origin. Prior prolonged bleeding history or elevated PTT may be the only clue to the diagnosis. Cardiac interventions can be performed after correction of the deficiency. FFP, factor XI concentrate and factor VII have
been used in the past. Presence of acquired inhibitor to factor XI, as a result of previous plasma infusion poses a major problem. Immunosuppressive therapy, plasma exchange and factor VII product transfusions have been used prior to cardiac interventions in few reported cases but the literature is limited.

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References