Case Report

A Rare Cause of Coagulopathy in a Patient with Rapidly Progressive Renal Failure

Abstract

Deranged coagulogram is a common problem, which a nephrologist faces before doing a renal biopsy. We describe a rare cause of coagulopathy in a patient with rapidly progressive renal failure due to acquired factor X deficiency caused by systemic light chain amyloidosis (AL). The patient had prolonged prothrombin and activated partial thromboplastin time, which got corrected on mixing with normal plasma, and factor X activity was markedly reduced at 5%. Rectal biopsy and immunofixation electrophoresis established the diagnosis of AL and the patient was started on bortezomib-based chemotherapy. Hence, appropriate coagulation work-up should be conducted in patients with renal dysfunction with prolonged coagulation times, as it can sometimes reveal the underlying diagnosis in situations where renal biopsy could not be done due to high risk of bleeding.

Keywords: *Coagulopathy, factor X deficiency, light chain amyloidosis*

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Introduction

Acquired factor X deficiency is the most common coagulation factor deficiency seen in patients with light chain amyloidosis (AL).[1,2] A study from Boston showed that 8.7% of patients with systemic AL had factor X deficiency.[3] The mechanism proposed for coagulopathy is the adsorption of amyloid fibrils to factor X in the liver and spleen.[4] Here we present a patient with rapidly progressive renal failure where evaluation of deranged coagulogram eventually led us to diagnosis of light chain AL.

Case Description

A 47-year-old female was admitted to our hospital with complaints of progressive swelling of both feet and facial puffiness for one month duration. Laboratory evaluation revealed serum creatinine of 8 mg/dL and normal size kidneys. The patient had deranged coagulogram on multiple occasions. The patient denied any history of prolonged bleeding, family history of bleeding, fever, joint pains, recurrent miscarriages, or use of antiplatelet/anticoagulants. Examination revealed pedal edema and multiple bruises at prick sites. However, no organomegaly was noted, and the rest of the systemic examination was unremarkable. Laboratory parameters revealed hemoglobin of 10.9 g/dL, total leukocyte count of 4900 cells/mm^3, platelet count of 4.5 lakhs/mm^3, serum urea of 165 mg/dL, and serum creatinine of 7.7 mg/dL. Urinalysis revealed 3+ albumin and one to two pus cells with 24-h urine protein excretion of 2.8 g/day. Serum total protein value was 5.4 g/dL, serum albumin 2.01 g/dL (A: G ratio 0.59), serum alkaline phosphatase 610 U/L, and the rest of the liver functions were normal. Coagulogram revealed prothrombin (PT) of 57.4 s (normal range: 11–13 s) and activated partial thromboplastin time (APTT) of 43.4 s (normal range: 25–35 s). Coagulopathy did not improve after infusions of fresh frozen plasma (FFP) at doses of 15 mg/kg for 3 days and vitamin K parenteral injections. Her D-dimer and serum fibrinogen levels were within normal limits ruling out disseminated intravascular coagulation. Antinuclear antibody, lupus anticoagulant, anticardiolipin antibody, and anti- β2 glycoprotein antibody were negative. Ultrasound of abdomen revealed no evidence of chronic liver disease. PT and APTT mixing studies were done and were corrected to normal suggesting clotting factor deficiency. Factor X assay was done and it was severely low at 5% (normal range: 70%–120%). This factor deficiency

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Table 1: Causes of coagulopathy in a patient of rapidly progressive renal failure

PT	APTT	Cause
Prolonged	Normal	Vit. K deficiency, liver disease, isolated factor VII deficiency
Normal	Prolonged	APLA nephropathy, heparin use in hemodialysis, factor VIII, IX, X, XI deficiency
Prolonged	Prolonged	Sepsis, liver disease, oral anticoagulant, factor V, VII, X, II deficiency

PT: Prothrombin; APTT: Activated partial thromboplastin time; APLA: Antiphospholipid antibody syndrome

was presumed to be acquired, as there was no personal or family history of bleeding. Serum protein electrophoresis showed monoclonal band (quantified to be 0.6 g/dL) that was subtyped as Kappa by immunofixation electrophoresis. Serum free kappa light chains were elevated to 422 mg/L (normal range: 3.3–19.4 mg/L) and lambda free light chains were normal at 9.34 mg/L (normal range: 5.7–26.6mg/L) while bone marrow examination showed only 3% plasma cells. Skeletal survey did not reveal any lytic lesions. Abdominal fat pad aspirate for amyloid was negative twice; however, rectal biopsy done under FFP cover showed acellular congophilic material that showed apple green birifrengence on polarizing microscopy suggestive of amyloid. Hence, a diagnosis of light chain systemic AL with acquired factor X deficiency was made and the patient was started on cyclophosphamide, bortezomib, dexamethasone, and thalidomide-based chemotherapy. Renal biopsy could not be done in view of persistent coagulopathy and renal dysfunction was presumed to be due to renal AL. Transjugular renal biopsy was considered, but the patient refused due to logistic reasons.

Discussion

Coagulopathy is a common problem encountered by a nephrologist. Here we have described causes, brief approach, and evaluation of a patient with deranged coagulogram [Table 1]. Moderate to severe coagulopathy (PT or APTT more than 1.5 times upper limit of normal) in patients planned for renal biopsy needs thorough evaluation. If coagulopathy persists after excluding sepsis, liver disease, and vitamin K supplementation (15 mg/Kg for three days), mixing study should be done next. If coagulation parameter improves after mixing study, it suggests inherited or acquired factor deficiency and warrants a functional factor assay as done in our patient. Failure of coagulogram to correct after mixing study suggests clotting inhibitor in patient's plasma, and further tests for lupus anticoagulant and anticardiolipin antibody should be done.

Many causes of bleeding tendencies in systemic AL are postulated that include acquired coagulation factor deficiencies, abnormal fibrin polymerization, hyperfibrinolysis, platelet functional defect, and amyloid deposits *per se* causing increased vascular fragility and vasoconstriction.[5,6] Factor X deficiency is the most common coagulation factor defect seen in systemic AL, in 8.7%–14% of patients.[3] Deficiencies of other coagulation factors such as II, V, VII, and IX have been rarely reported.[7] Factor X deficiency causes prolongation of both PT time and APTT as its function is to catalyze the generation of thrombin from PT as seen in our patient.

The half-life of factor X is shortened in AL as it gets adsorbed by the amyloid fibrils.[4] PT complex concentrate, FFP, and recombinant factor VIIa have been used in the treatment of factor X deficiency with mixed results.[8] Correction of coagulogram with FFP was attempted in our case but was not completely successful, which could be attributed to the fact that factor X is rapidly cleared from the blood by the amyloid fibrils and there are other causes of prolonged coagulation in AL as described earlier. Splenectomy has also been shown to improve coagulopathy by removing significant burden of amyloid fibrils.[9] Finally, chemotherapy with high-dose melphalan followed by autologous stem-cell transplant has been shown to revert factor X deficiency.[10]

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Conclusion

Abnormal coagulation parameters need thorough evaluation in a case of unexplained renal failure as it can give clue to underlying diagnosis.

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Conflicts of interest

There are no conflicts of interest.

References

1. Girmann G, Wilker D, Stadie H, Scheurlen PG. Acquired isolated factor X deficiency associated with systemic amyloidosis. Case report and review of literature. Klin Wochenschr 1980;58:859-62.
2. Greipp PR, Kyle RA, Bowie EJ. Factor-X deficiency in amyloidosis: A critical review. Am J H ematol 1981;11:443-50.
3. Choufani EB, Sanchorwala V, Ernst T, Quillen K, Skinner M, Wright DG, *et al*. Acquired factor X deficiency in patients with amyloid light-chain amyloidosis: Incidence, bleeding

manifestations and response to high-dose chemotherapy. Blood 2001;97:1885-7.

4. Furie B, Greene E, Furie BC. Syndrome of acquired factor X deficiency and systemic amyloidosis: *In vivo* studies of the metabolic fate of factor X. N Engl J Med 1977;297:81-5.
5. Gamba G, Montani N, Anesi E, Palladini G, Capezzera M, Soldavini E, *et al*. Clotting alterations in primary systemic amyloidosis. Haematologica 2000;85:289-92.
6. Mumford AD, O'Donnell J, Gillmore JD, Manning RA, Hawkins PN, Laffan M. Bleeding symptoms and coagulation abnormalities in 337 patients with AL-amyloidosis. Br J Haematol 2000;110:454-60.
7. McPherson RA, Onstad JW, Ugoretz RJ, Wolf PL. Coagulopathy in amyloidosis: Combined deficiency of factors IX and X. Am J Hematol 1977;3:225-35.
8. Thompson CA, Kyle R, Gertz M, Heit J, Pruthi R, Pardanani A. Systemic AL amyloidosis with acquired factor X deficiency: Astudy of perioperative bleeding risk and treatment outcomes in 60 patients. Am J Hematol 2010;85:171-3.
9. Rosenstein ED, Itzkowitz SH, Penziner AS, Cohen JI, Mornaghi RA. Resolution off actor X deficiency in primary amyloidosis following splenectomy. Arch Intern Med1983;143:597-9.
10. Camoriano JK, Greipp PR, Bayer GK, Bowie EJ. Resolution of acquired factor X deficiency and amyloidos is with melphalan and prednisone therapy. N Engl J Med 1987;316:1133-5.