Patient with lupus anticoagulant caused aPTT prolongation corrected with prednisolone treatment and later anticoagulation treatment due to chronic atrial fibrillation.

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Abstract

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CASE REPORT

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A KEY CLINICAL MESSAGE

Lupus anticoagulant caused aPTT prolongation in rare case can cause bleeding tendency especially when combined with other hemostasis abnormalities. In such cases aPTT value can be corrected by immunosuppressants within several days of treatment. When anticoagulation therapy is needed vitamin K antagonist are a good option for treatment.

ABSTRACT

Lupus anticoagulant antibodies despite causing aPTT prolongation are commonly associated with increased risk of thrombosis. We present a rare case of patient when these autoantibodies resulted in dramatic aPTT prolongation and combined with associated thrombocytopenia resulted in minor bleeding events. In presented case treatment with oral steroids resulted in aPTT values correction followed by resolution of bleeding tendency within several days. Later the patient developed chronic atrial fibrillation and was started on anticoagulation treatment with vitamin K antagonist without bleeding complications during follow-up period. Corresponding changes in patient's aPTT time in a course of whole treatment is presented.

KEY WORDS

lupus anticoagulant, bleeding, aPTT prolongation, case report

INTRODUCTION

Coagulation screening prior to surgery or any other invasive procedure is performed routinely to identify patients with increased bleeding risk. Isolated prolongation of activated partial thromboplastin time (APTT) is not common finding in general population and it is most often attributable to anticoagulant therapy(1) or antiphospholipid antibodies. Less common reasons include deficiencies of a factor of the contact pathway, deficiencies of factors of the intrinsic and common pathways, von Willebrand disease, liver disease/vitamin K deficiency, hypofibrinogenemia, disseminated intravascular coagulation and supercoumarin intoxication(2).

Lupus anticoagulant is a class of antiphospholipid antibody causing a phospholipid-dependent prolongation of the clotting time but is not usually associated with bleeding tendency but rather with increased risk of thrombosis and pregnancy morbidity. Lupus anticoagulant is regarded as rare case of bleeding(3,4) with few examples that can be found in literature (2,5). In special cases lupus anticoagulant caused aPTT prolongation can be also associated with acquired factor II deficiency causing lupus anticoagulant-hypoprothrombinemia syndrome which is a rare disease predisposing to severe bleeding(6,7).

CASE PRESENTATION

A 64-year-old woman was referred to our hospital by nephrologist due to observed nephrotic proteinuria. The patient had a history of systemic lupus erythematosus diagnosed 30 years ago with cutaneous lesions and arthritis treated with glucocorticosteroids and chloroquine without any documented further relapses. Her past medical history included chronic kidney disease stage G3/G4, gout, hypertension, complex heart defect correction - implantation of pericardial mitral bioprosthesis and tricuspid valve repair (2010), traffic accident (2014) followed up by skin grafts (2015, 2016), abdominal hernia repair (2016) and cholecystectomy.

6 months before the patient had proteinuria of 2.5 g/day which increased to 6.75 g/day with stable serum creatinine level and periodically observed lower extremity oedema. Additionally the patient complained of several episodes of epistaxis. With the suspicion of lupus nephropathy the patient was admitted for kidney biopsy. She had slight lower extremity oedema and elevated blood pressure 195/96 mmHg. Her laboratory tests revealed an isolated prolongation of aPTT to maximum value of 172.6 sec (normal range 22.6 – 34 sec), slight normochromic anemia (hemoglobin 11 g/dL), thrombocytopenia (115 10ˆ3/µL), elevated serum creatinine (170 µmol/L), ESR 75 mm/1h (normal <20), parathormone (147 ng/L) and TSH levels (7.670 mIU/L). Due to observed abnormalities in coagulation tests and tendency to extended bleeding, bruising and epistaxis patient was disqualified from kidney biopsy because of the high risk of bleeding. Further coagulation tests were performed. 1:1 mixing study showed no aPTT correction (107.9 sec) what suggested a presence of anticoagulant or inhibitor of factor VIII. Serum levels of factor VIII, IX, XI and XII were normal. Lupus anticoagulant test was positive at high titers along with positive anti-dsDNA antibodies and ANA level of 1:1280. Anticardiolipin and anti-beta 2-glycoprotein I antibodies were found negative. Systemic lupus erythematosus relapse was diagnosed. After exclusion of infections sites the therapy with prednisone was started (60 mg of prednisolone per day). After five days of treatment the aPTT decreased to 100.8 sec. The previously observed tendency to bleeding was resolved. After 30 days of treatment aPTT

decreased to 40.5 sec. Because diabetes was diagnosed after two months of prednisolone treatment, the dose was reduced and the therapy with mycophenolate mofetil was started.

Four months later the patient had to be admitted to the hospital because of symptoms of chronic heart failure i.e. general malaise, increasing lower extremity oedema, heart palpitations and chest pain. Atrial fibrillation was diagnosed with rapid ventricular response 130-140/min. Increased natriuretic peptides were found and serum creatinine increased to 232 μmol/L. Echocardiography showed enlarged left atrium. Despite of implemented treatment atrial fibrillation did not convert to sinus rhythm. Due to implemented treatment with good control of heart rate the patient's condition improved significantly. Four months after the start of treatment aPTT was 50 sec and proteinuria was 3.59 g/day. Because of the high risk of ischemic stroke associated with atrial fibrillation an anticoagulation treatment was started. Low molecular weight heparin was contraindicated because of persistent thrombocytopenia and high risk of heparin-induced thrombocytopenia (HIT). Treatment with NOAC (non-vitamin K antagonist oral anticoagulants) was also contraindicated because of its impact on aPTT, which was used to control the treatment of SLE. Therefore, the treatment with acenocumarol, a vitamin K antagonist (VKA), was started.

During the period of follow-up no bleeding were observed. Table 1 presents aPTT before treatment, during immunosuppressive therapy and during the therapy with acenocumarol.

Table 1 . Changes of patient's aPTT during treatment

Day of tretament	Therapheutic option	Patient's aPTT (sec) [normal 22 - 34]
0	Before treatment	172.6
3	3'rd day of prednisolone (60 mg)	151.1
5	5'th day of prednisolone (60 mg)	100.8
30	One month of prednisolone (60 mg)	40.5
60	Two months of prednisolone (60mg)	36.8
100	Two weeks of Mycophenolate Mofetil* + GKS**	43.7
120	Two months of Mycophenolate Mofetil* + GKS**	48.6
130	One week of VKA + Mycophenolate Mofetil* + GKS**	41.5

* - Mycophenolate Mofetil dose was 500 mg twice per day

** - prednisolone in reducing dosage

DISCUSSION

In this case report, we present the case of patient with systemic lupus erythematosus with nephrotic syndrome and increased aPTT due to lupus anticoagulant. The observed bleeding could be associated with thrombocytopenia, however it disappeared with decreasing of aPTT despite persisting thrombocytopenia. The immunosuppressive treatment with prednisolone corrected aPTT. In this case the transfusion of serum would not improve aPTT as it was reflected in aPTT mixing study results. Because of increased aPTT we were not able to do the kidney biopsy. Renal biopsy was crucial to diagnose a specific form and stage of lupus nephritis. Kidney biopsy should be done in all patients with lupus nephritis and nephrotic range proteinuria (8). Reduced prednisolone dose with mycophenolate mofetil treatment have the same impact on aPTT than treatment with high dose of prednisolone alone. Proteinuria decreased during the immunosuppressive therapy however no decreased of serum creatine during the follow-up period was observed. New onset atrial fibrillation was observed in the patient during the therapy. Due to the high risk of stroke associated with atrial fibrillation, anticoagulant therapy was necessary. Choice of anticoagulation treatment was limited due to NOAC influence on aPTT assay(9) and concern for the high risk of HIT development(10). The initiated vitamin K antagonist therapy did not interfere with aPTT and did not cause any bleeding during the follow-up period.

CONCLUSION

Bleeding complications although rare have to be taken into account in patients with lupus anticoagulant. Increased aPTT can be observed in those patients combined with other coagulation disorders i.e. thrombocytopenia or acquired factor II deficiency. Anticoagulation treatment in SLE patients might be a challenge because of limited treatment options.

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AUTHOR CONTRIBUTIONS

MF, PP, AK were actively involved in the clinical care of the patient. MF wrote the manuscript. PP, AK and DM revised the manuscript.

CONFLICT OF INTEREST

The authors confirm that this article content has no conflict of interest.

REFERENCES

1. Tagariello G, Radossi P, Salviato R, et al. Clinical relevance of isolated prolongation of the activated partial thromboplastin time in a cohort of adults undergoing surgical procedures. Blood Transfus. 2017 Oct;15(6):557-561. doi: 10.2450/2016.0047-16.
2. Barbosa ACN, Montalvão SAL, Barbosa KGN, Colella MP, Annichino-Bizzacchi JM, Ozelo MC, De Paula EV. Prolonged APTT of unknown etiology: A systematic evaluation of causes and laboratory resource use in an outpatient hemostasis academic unit. Res Pract Thromb Haemost. 2019 Sep 8;3(4):749-757. doi: 10.1002/rth2.12252.
3. Molhoek JE, de Groot PG, Urbanus RT. The Lupus Anticoagulant Paradox. Semin Thromb Hemost. 2018 Jul;44(5):445-452. doi: 10.1055/s-0037-1606190.
4. Boxer M, Ellman L, Carvalho A. The lupus anticoagulant. Arthritis Rheum. 1976 Nov-Dec;19(6):1244-8. doi: 10.1002/art.1780190603. PMID: 999735.
5. Li Y, Lyu Me, Xue F, et al. Lupus anticoagulant: two cases report and literature review. Zhonghua Xue Ye Xue Za Zhi. 2016 Feb;37(2):130-3. Chinese. doi: 10.3760/cma.j.issn.0253-2727.2016.02.009.
6. Meireles E, Machado F, Teles L, Chumakova A, Sequeira J, Spínola A. A case report of severe bleeding due to lupus anticoagulant hypoprothrombinemia syndrome. J Thromb Thrombolysis. 2020 Feb;49(2):334-336. doi: 10.1007/s11239-019-01955-1.
7. Mazodier, Karin MD; Arnaud, Laurent MD, PhD; Mathian, Alexis MD, et al. Lupus Anticoagulant-Hypoprothrombinemia Syndrome. Medicine. 2012 Sep;91(5):251-260 doi: 10.1097/MD.0b013e31826b971f
8. Musa R, Brent LH, Qurie A. Lupus Nephritis. StatPearls. 2021 Aug. Treasure Island (FL): StatPearls Publishing.
9. Ji Q, Xu Q, Wang Z, Li X, Lv Q. Association between activated partial thromboplastin time, age and bleeding events in NVAF patients receiving dabigatran. Eur J Clin Pharmacol. 2019 Mar;75(3):321-328. doi: 10.1007/s00228-018-2583-5.
10. Hogan M, Berger JS. Heparin-induced thrombocytopenia (HIT): Review of incidence, diagnosis, and management. Vasc Med. 2020 Apr;25(2):160-173. doi: 10.1177/1358863X19898253.