Journal of Case Reports and Studies
Volume 5 | Issue 6
ISSN: 2348-9820
Case Report Open Access

Acquired Factor XII Deficiency in a Patient with Schizophrenia

Dehghan-Nayeri N[1], Moazezi-Nekooi-Asl S[2] and Malek F[*1]

[1]Pediatric Congenital Hematologic Disorders Research Center, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran
[2]Iranian Comprehensive Haemophilia Care Center, Tehran, Iran

[*]**Corresponding author:** Malek F, Pediatric Congenital Hematologic Disorders Research Center, Mofid children's Hospital, Shariati Ave, Tehran, Iran, Fax: (+98-21) 22265488, Tel: (+98-21) 22904536, E-mail: fmalek7721@gmail.com

Citation: Dehghan-Nayeri N, Moazezi-Nekooi-Asl S, Malek F (2017) Acquired Factor XII Deficiency in a Patient with Schizophrenia. J Case Rep Stud 5(6): 602

Received Date: November 18, 2017 **Accepted Date:** December 27, 2017 **Published Date:** December 29, 2017

Abstract

We report a 50-year-old man who presented schizophrenia and an abnormal coagulation profile indicative of an inhibitor. Clinical experiments demonstrated prolonged partial thromboplastin time along with acquired factor XII deficiency and a positive anticoagulant antibody. To the best of our knowledge, the coexistence of schizophrenia and anticoagulant antibody with deficiency of coagulation factor XII is extremely rare that has not previously been reported. This patient has also indicated the paraplegia associated with spinal tuberculosis along with the loss of bladder and bowel control. Herein, we present the case of a chronic schizophrenia patient who developed the anticoagulant antibody and abnormally low serum levels of factor XII.

Keywords: Schizophrenia; Autoimmunity; Tuberculosis; Coagulopathy; Acquired Factor XII Deficiency

Introduction

Factor XII, also called Hageman factor, plays an essential role in the thrombosis. Studies demonstrated lack of Factor XII is not associated with a bleeding tendency [1]. Previous studies evidenced that FXII antibodies exist in significant numbers of patients with antiphospholipid syndrome and may lead to acquired FXII deficiency [2]. Whereas factor XII deficiency is totally asymptomatic, it is often detected accidentally. On the other hand, schizophrenia is known as a complex neurodevelopmental disorder that various molecular pathways are involved in its pathogenesis. Recently, it has been demonstrated the link between hemostatic process and pathogenesis of schizophrenia [3]. Additionally, a protein-protein interaction study revealed the relationship between coagulation factor genes (III, VII and X) and antipsychotic-associated genes [4]. Overall, existing studies show a clear correlation between schizophrenia and coagulation function. Herein, we provide a brief overview of the patient with schizophrenia and coagulation disorders to consider parallel approaches being used to express the molecular causes of schizophrenia and discuss possible directions for future researches.

Case description

A 50-year-old man diagnosed with schizophrenia was presented to the coagulation clinic because of 6-months aPTT prolongation. The patient had a 40-year history of schizophrenia and the treated tuberculosis 3 years ago along with developed urinary and fecal incontinence with paraplegia after tuberculosis until now. Given his past history, he had no previous history of the bleeding disorders. The primary laboratory testing demonstrated a normal complete blood count and prothrombin time, but he had a prolonged activated partial thromboplastin time. Moreover, coagulation experiments showed a low level of coagulation factors XI and XII (Table 1). According to the results of the mixing test, a 1:1 mixture of the patient's plasma with pooled normal plasma, the prolonged aPTT remained uncorrected. We subsequently evaluated the presentation of factor-specific inhibitors (VIII, IX, XI and XII) that were negative. Finally, we suspected the lupus anticoagulant and results showed the presence of this autoantibody. Immunoglobulin examination (IgG and IgM) was found to be negative. The routine biochemical examination was normal. Kidney and liver functioned normally. No tumor thrombus was found in the portal vein, the hepatic vein trunk and the inferior vena cava. His parents didn't have consanguineous marriage. Totally, the current presentation has explained some episodes of rare diseases in one case. In the following, we assess the relationship between theses serial diseases and their possible causes.

Test	Result	Reference interval
aPTT, s		
Patient	83 *	28-38
Pooled normal plasma	34	28-38
Mixture (1:1), s	61 *	28-38
PT, s		
Patient	11.5	10-13
Pooled normal plasma	10	10-13
Mixture (1:1), s	11	10-13
Factor activities, %		
FVIII	89	50-150
FIX	100	50-150
FXI	45 *	50-150
XII	28 *	50-150
XIII screen	Normal	
Fibrinogen, mg/dL (mol/L)	4.32	1.5-4.5
Factor inhibitors		
FVIII	Negative	
FIX	Negative	
FXI	Negative	
XII	Negative	
Lupus anticoagulant	Positive *	
IgG	3	<10
IgM	4.25	<10
Antithrombin III	104.9	80-120
Protein S	112.1	63-140
Protein C	110.3	70-130

Table 1: Patient's laboratory results (citrated plasma)

Discussion

It is very rare that a patient be involved in two different classes of disorders, schizophrenia as a neurodevelopmental disorder and factor deficiency as a coagulation disorder, simultaneously. But in fact, both classes of disorders can present a spectrum of genotypes overlapping; therefore, it is likely that the genetic mutations in the specific pattern can cause developing the both disorders [5]. Presented schizophrenia case has revealed a persistent mild decrease of clotting factor XII with positivity for lupus anticoagulant and normal values of IgG and IgM anticardiolipin antibodies. According to the previous studies, immune dysfunction may contribute to the pathogenesis of psychiatric diseases such as schizophrenia in the field of Neuroimmunology [6]. Overall, two general reasons can consider for positive lupus anticoagulant in the schizophrenia patients, firstly, brain inflammation as well as damage to the membrane of brain cells that can induce autoantibodies production [7], secondly, drug-induced lupus anticoagulant can be resulted from long term use of certain medications, such as phenothiazines. These findings trigger questions regarding what disorders can be result following the schizophrenia-induced autoimmunity. Previous studies showed that the incidence rate of tuberculosis is remarkably higher in schizophrenic patients than that of the general population [8]. In fact, schizophrenia has been considered as an important risk factor for tuberculosis. The molecular basis of the comorbidity between schizophrenia and tuberculosis is currently unclear. However, recent evidence suggests that autoimmunity is a critical process in tuberculosis pathogenesis [9], therefore, it seems schizophrenia-induced autoimmunity can be considered as a central process in development of tuberculosis and consequently comorbidity of schizophrenia and tuberculosis. Nevertheless, immune dysfunction can be exist in the both of schizophrenia and tuberculosis and can help to elucidate the common molecular mechanisms of the both diseases.

On the other hand, a decrease in the blood coagulation factors, including factor XI and factor XII, were found in this patient. The alterations in coagulation and fibrinolysis processes are known to be involved in some cases with psychiatric disorders, such as schizophrenia [10]. Additionally, biological mechanisms of hypercoagulability and hypofibrinolysis can develop hypercoagulable state which is known as an important factor in developing thromboembolism in some schizophrenia patients [10]. Previous studies have shown associations between tPA activity, C and S proteins level, and thromboembolism risk in schizophrenia patients [3]. There is no evidence of a direct relationship between schizophrenia and coagulation factors. However, evidence indicates that acquired FXII deficiency can be resulted from the infection diseases and or the autoimmune disorders [11]. Therefore, there

are two hypotheses for coagulation disorder in this patient, firstly, tuberculosis like the other chronic infections can develops alterations in the hemostatic mechanism. Previous researches have shown that tuberculosis is associated with the hypercoagulable state as reflected by enhanced activation of coagulation factors VIII and V and moderate decreased of FXI and FX [12]. Secondly, lupus anticoagulant as a heterogeneous group of autoantibodies can induce acquired FXII deficiency [2]. Overall, we cannot declare that primary schizophrenia directly causes acquired FXII deficiency or a schizophrenia-related secondary disorder such as tuberculosis or lupus anticoagulants. On the other hand, it has been demonstrated that reduced levels of FXII and presence of lupus anticoagulant are should be considered as the significant risk factors in the development of thromboembolism [13]. Although the exact mechanism of the thromboembolism in schizophrenia is not clear, but the coagulation pathway can establish as an important extra link between schizophrenia and coagulopathy-induced thromboembolism.

Conclusion

In conclusion, the schizophrenia does not seem to be the direct cause of the autoimmune dysfunction, but the gene overlapping can be considered as an important piece in the puzzle of schizophrenia-induced autoimmunity. This induced autoimmunity may increase the risk of developing other disorders such as tuberculosis and or coagulopathy. Finally, it should be noted that the exact reason for the occurrence of the three disorders in the same patient is not clear and all hypotheses in this article should be proven through the more studies.

Conflict of interest

The authors confirm that there are no conflicts of interest.

Ethical approval

This article does not contain any studies with human participants performed by any of the authors.

Informed consent

Written informed consent was obtained from the family members of the patient for publication of this Case report and any accompanying images.

Acknowledgments

The authors would like to thank Mr. M. Jazebi as head of laboratory and Ms. M. Hajati as laboratory technician at Iranian Comprehensive Hemophilia Care Center.

References

1. Shin D-Y, Lee H-R, Kang HJ, Na II, Chang YH, et al. (2015) Prevalent factor XII deficiency in cancer patients with isolated aPTT prolongation. Blood Res 50: 114-7.

2. Jones DW, Gallimore MJ, Harris SL, Winter M (1999) Antibodies to factor XII associated to lupus anticoagulant. Thromb Haemost 81: 387-90.

3. Hoirisch-Clapauch S, Amaral OB, Mezzasalma MA, Panizzutti R, Nardi AE (2016) Dysfunction in the coagulation system and schizophrenia. Transl Psychiatry 6: e704.

4. Huang KC, Yang KC, Lin H, Tsao TT, Lee SA (2014) Transcriptome alterations of mitochondrial and coagulation function in schizophrenia by cortical sequencing analysis. BMC Genomics 15: S6.

5. Kozol RA, Abrams AJ, James DM, Buglo E, Yan Q, et al. (2016) Function over form: modeling groups of inherited neurological conditions in zebrafish. Front Mol Neurosci 9: 55.

6. Needham E, Zandi MS (2014) Recent advances in the neuroimmunology of cell-surface CNS autoantibody syndromes, Alzheimer's disease, traumatic brain injury and schizophrenia. J Neurol 261: 2037-42.

7. Ermakov EA, Smirnova LP, Parkhomenko TA, Dmitrenok PS, Krotenko NM, et al. (2015) DNA-hydrolysing activity of IgG antibodies from the sera of patients with schizophrenia. Open Biol 5: 10.1098/rsob.150064.

8. Kuo SC, Chen YT, Li SY, Lee YT, Yang AC, et al. (2013) Incidence and outcome of newly-diagnosed tuberculosis in schizophrenics: a 12-year, nationwide, retrospective longitudinal study. BMC Infect Dis 13: 351.

9. Elkington P, Tebruegge M, Mansour S (2016) Tuberculosis: An Infection-Initiated Autoimmune Disease? Trends Immunol 37: 815-8.

10. Chow V, Reddel C, Pennings G, Scott E, Pasqualon T, et al. (2015) Global hypercoagulability in patients with schizophrenia receiving long-term antipsychotic therapy. Schizophr Res 162: 175-82.

11. Kumar R, Gupta A, Mathur P, Garg M (2016) Factor XII deficiency - A rare coagulation disorder. Indian J Child Health 3: 349-50.

12. Kager LM, Blok DC, Lede IO, Rahman W, Afroz R, et al. (2015) Pulmonary tuberculosis induces a systemic hypercoagulable state. J Infect 70: 324-34.

13. Windyga J (2002) Antiphospholipid antibodies as risk factor for venous thromboembolism. Pol Arch Med Wewn 108: 1065-70.