COMMUNICATION COURTE

Un syndrome lupus anticoagulant-hypoprothrombinémie acquise transitoire chez un enfant

A transient acquired lupus anticoagulant-hypoprothrombinemia syndrome in a child

Meriem Hadhri[1]
Hela Baccouche [1,2]
Aya Chakroun[1,2]
Sonia Mahjoub[1,2],
Neila Ben Romdhane[1,2]

1 Hematology Department, La Rabta University Hospital, Tunis, Tunisia

2 Faculty of Medicine of Tunis, Tunis University El Manar, Tunis, Tunisia

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Correspondent author:
Meriem Hadhri,
Biologist Doctor,

Address :
Hematology Department, La Rabta University Hospital, Jabbari 1007 Tunis, Tunisia

E-mail :
hadhrimeriem@yahoo.com

Résumé

Introduction
Le syndrome lupus anticoagulant-hypoprothrombinémie est une maladie rare qui touche principalement les enfants. Il peut prédisposer à des hémorragies sévères causées par des anticorps anti-prothrombine. Il est souvent associé à une dysimmunité ou à une infection virale.

Objectif
Nous rapportons le cas d'un syndrome lupus anticoagulant-hypoprothrombinémie chez un enfant de 3 ans consultant pour des manifestations hémorragiques minimes avec notion d'infection virale quelques jours auparavant.

Méthodes
Le plasma déplaquetté a été obtenu par une double centrifugation d'un sang total citraté. Le taux de prothrombine, le temps de céphaline avec activateur, les tests de mélange avec un plasma témoin et le dosage des facteurs de la coagulation ont été réalisés. La recherche du lupus anticoagulant a été réalisée. La recherche des anticorps anti-cardiolipineet des anti-Béta-2-glycoprotéine 1 a été faite avec des tests ELISA.

Résultats
Les évaluations biologiques initiales ont révélé un allongement des tests de coagulation : taux de prothrombine et temps de céphaline avec activateur, et les bilans biologiques complémentaires ont montré la présence d'un lupus anticoagulant et un déficit en facteur II. Un mois plus tard, le patient a eu une résolution spontanée.

Conclusion
Le syndrome lupus anticoagulant-hypoprothrombinémie doit être suspecté chez tout enfant qui présente des manifestations hémorragiques et/ou un allongement des tests de coagulation, amenant au dépistage du lupus anticoagulant et au dosage du facteur II.

Mots clés : *Lupus anticoagulant, hypoprothrombinémie acquise, infection transitoire*

Abstract

Introduction
Lupus anticoagulant-hypoprothrombinemia syndrome is a rare disorder that mostly occurs in pediatric patients. It may predispose to severe bleeding caused by the production of prothrombin antibodies. The disease is often associated with autoimmunity or viral illness.

Objective
We report a case of 3-year-old child having a lupus anticoagulant-hypoprothrombinemia syndrome with mild bleeding symptoms and a previous infection few days before their appearance.

Methods
Platelet poor plasma was prepared by double centrifugation of the citrated whole blood. Prothrombin time, activated partial thromboplastin time, thrombin time, correction of coagulation tests after 1:1 mixing with normal plasma and factor clotting activities were measured using reagents from STAGO. Rosner index was calculated. Screening for lupus anticoagulant was also investigated (STA-STACLOT and DRVVT; STAGO, France). Search of anti-cardiolipin and anti-beta2glycoprotein 1 was performed with ELISA method.

Results
Initial evaluations revealed prolonged coagulation tests: prothrombin time and activated partial thromboplastin time and further laboratory investigations demonstrated the presence of lupus anticoagulant and a factor II deficiency. One month later, the patient had a spontaneous resolution: prothrombin time, activated partial thromboplastin time and factor II activity were normal, and the screening for the lupus anticoagulant was negative.

Conclusion
Lupus anticoagulant-hypoprothrombinemia syndrome should be suspected in any child with bleeding symptoms and/or prolonged coagulation tests leading to the screening of lupus anticoagulant and the measurement of factor II activity.

Key words: *Lupus anticoagulant, acquired hypoprothrombinemia, transient infection*

INTRODUCTION

Lupus anticoagulant-hypoprothrombinemia syndrome (LAHPS) is a rare entity comprising the presence of lupus anticoagulant and acquired hypoprothrombinemia related to prothrombin antibodies. It mostly occurs in young females and more specifically in children (1-6). These antibodies, unlike other prothrombotic antiphospholipid antibodies, promote bleeding (3, 4). LAHPS is usually associated with autoimmune disease (such as systemic lupus erythematosus, antiphospholipid antibody syndrome and celiac disease) or transient viral infection (1, 3). As this entity is misdiagnosed, we reported a transient acquired lupus anticoagulant-hypoprothrombinemia syndrome in a 3-year-old child with mild bleeding manifestations but unexpected prolonged coagulation tests.

CASE REPORT

A 3-year-old child presented with ecchymotic lesions in the legs which appeared three weeks previously. He had no personal or familial history of bleeding but a rhinitis few days ago. Physical examination was normal except one-centimeter ecchymosis regarding to the tibia. Blood count showed normal platelet count at 200.000/mm^3 (reference range 150.000-400.000/mm^3). Initial coagulation tests were as following: Prothrombin Time (PT) was 16.5 s (normal value 11.5 s), Activated Partial Thromboplastin Time (APTT) was 64.7s (normal value 35 s), Thrombin Time was 32.4s (normal value 20 s) and fibrinogen level was 2.61 g/L (reference range 2-4 g/L). Mixing the plasma with an equal volume of normal plasma did not correct the prolonged APTT (Rosner index was 45.5%) but corrected the PT. Measurement of clotting factor activities revealed an isolated FII deficiency (37.5%; reference range 60-130%). The other factors were normal: FV=119%, FVII=61% and FX=91% (reference range 60-130% for all factors). Further investigations revealed that his parents had normal level of FII. LAHPS was therefore suspected. The screening of Lupus Anticoagulant (LA), performed according to the International Society of Thrombosis and Hemostasis (ISTH) recommendations using two reagents: STA APTT and DRVVT SCREEN (STAGO; Asnières; France), was positive. The phospholipid dependence was confirmed by positive phospholipid-neutralizing assays for both tests with STACLOT LA and STA-DRVVT CONFIRM (STAGO; France). In addition, anti-cardiolipin and anti-β 2 glycoprotein 1 antibodies investigated with Enzyme Linked Immunosorbent Assay (ELISA) method were negative. As the patient had mild bleeding, no treatment was introduced. One month later, PT, APTT and FII level were normal and the LA screening was negative.

DISCUSSION

This patient was pauci-symptomatic. Initial coagulation tests showed a prolongation of both PT and APTT and a decrease of factor II activity with correction of PT and factor II and no correction of APTT on mixing studies. Further investigations excluded a familial deficiency in factor II and revealed the presence of LA. Our patient had a previous rhinitis few days before the appearance of symptoms with a spontaneous resolution one month later, orienting the diagnosis toward LAHPS associated with viral infection. In fact, infection associated LAHPS is commonly seen in children < 10 years of age and is usually transient and self-limited with minor hemorrhagic manifestations. The most frequently reported viruses are adenovirus, cytomegalovirus, varicella and Epstein-Barr virus (2). On the contrary, LAHPS associated with autoimmune disease tends to occur in children older than 10 years of age with production of autoantibodies and is more persistent and less likely to disappear spontaneously and may predispose to severe bleeding requiring intensive

treatment (2, 5). The patient was pauci symptomatic which could be explained by moderate FII deficiency and normal platelet count. A review of the literature on reported cases of bleeding in children with acquired hypoprothrombinemia between 1960 and 2014 (2) revealed that factor II activity varies from < 1% to 56%. Bleeding risk is correlated to factor II levels and varies from mild manifestations to severe hemorrhagic complications (1) when factor II activity is less than 10% of normal (2, 5). It has been demonstrated that there are non-neutralizing anti-prothrombin (factor II) antibodies that lead to rapid clearance of antigen-antibody complexes in the reticuloendothelial system responsible for an acquired hypoprothrombinemia. These antibodies bind to inactive sites on the prothrombin antigen and so they do not affect the coagulant activity of normal plasma used in mixing studies (2). There are no standard recommendations for the treatment of LAHPS. The treatment is not necessary in asymptomatic patients or in those presenting minor bleeding as it is the case in this observation. In severe bleeding cases, a special therapy may be required consisting of transfusions with plasma and prothrombin complex concentrates to manage bleeding episodes and of immunosuppressive regimes (corticosteroids, intravenous immunoglobulin, Cyclophosphamide, Azathio-prine, Rituximab or plasmapheresis) to suppress the formation of antibodies (1, 2, 7).

CONCLUSION

In summary, although it is a rare disease, LAHPS is most common in pediatric patients and may expose to life-threatening bleeding. Therefore, it should be suspected in any child with bleeding symptoms and/or prolonged coagulation tests leading to the screening of LA and the measurement of factor II activity.

Disclosure of interest: The authors declare that there is no conflict of interest.

RÉFÉRENCES BIBLIOGRAPHIQUES

1. Appert-Flory A, Fischer F, Amiral J, Monpoux F. Lupus Anticoagulant-Hypoprothrombinemia Syndrome (HLAS): Report of one case in a familial infectious context. Thromb Res 2010; 126:e139-40.

2. Sarker T, Roy S, Hollon W, Rajpurkar M. Lupus anticoagulant acquired hypoprothrombinemia syndrome in childhood: two distinct patterns and review of the literature. Haemophilia. 2015; 21:754-760.

3. Bel Feki N, Zayet S, Ben Ghorbel I, Houman MH. Lupus anticoagulant-hypoprothrombinemia syndrome presenting with co-existing cerebral venous thrombosis and subdural hemorrhage. Journal des maladies vasculaires. 2016; 41: 403-406.

4. Ieko M, Yoshida M, Naito S, Ohmura K, Takahashi N. Lupus anticoagulant-hypoprothrombinemia syndrome and similar diseases: experiences at a single center in Japan. Int J Hematol. 2019; 110(2):197-204.

5. Foord A, Baca N, Buchbinder D, Mahajerin A. Lupus anticoagulant hypoprothrombinemia syndrome associated with severe thrombocytopenia in a child. Pediatr Blood Cancer. 2016; 64: e26357.

6. Vandamme S, Desclée E, Ver Elst K, Weekx S, Maes P, Van Brusselen D, *et al*. Lupus anticoagulant hypoprothrombinaemia syndrome: An instructive paediatric case. J Paediatr Child Health. 2021; 57(3):443-444.

7. Kocheril AP, Vettiyil GI, George AS, Shah S, Geevar T, Dave RG, *et al*. Pediatric systemic lupus erythematosus with lupus anticoagulant hypoprothrombinemia syndrome-A case series with review of literature. Lupus. 2021; 30(4):641-648.