

# LUPUS ANTICOAGULANT HYPOPROTHROMBINEMIA SYNDROME: A CASE REPORT

Natalia Acedo<sup>1</sup>, Alejandro Cabrero<sup>1</sup>, Eliana Samantha Feijóo<sup>1</sup>, Cristina García<sup>1</sup>, Ana M Ortiz<sup>1</sup>, and Adrián Alegre<sup>1</sup>

<sup>1</sup>Hospital Universitario de la Princesa

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## Abstract

Lupus anticoagulant hypoprothrombinemia síndrome (LAHPS) is a rare entity. A 54-year-old woman diagnosed with systemic lupus erythematosus (SLE) present in August 2020 with cerebellar haemorrhage, coagulation factor II deficiency was found. After increasing corticosteroid dose and adjustment of immunosuppressive therapy FII levels increased. She has no presented new haemorrhagic events.

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Natalia Acedo<sup>1</sup>, Alejandro Alonso<sup>1</sup>, Eliana Samantha Feijóo<sup>1</sup>, Cristina García<sup>1</sup>, Ana M Ortiz<sup>2</sup>, Adrián Alegre<sup>1</sup>

<sup>1</sup>Hematology Department, Hospital Universitario de La Princesa, Madrid, Spain

<sup>2</sup>Rheumatology Department, Hospital Universitario de La Princesa, Madrid, Spain

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## INTRODUCTION

Lupus anticoagulant hypoprothrombinemia syndrome (LAHPS) is a rare entity consisting of lupus anticoagulant (LA) positivity associated with an acquired deficiency of coagulation factor II (FII). The origin of this deficiency seems to be associated with acquired antibodies against FII (anti-FII) <sup>1</sup>. There is evidence of the presence of non-neutralizing anti-FII antibodies in the plasma of these patients with accelerated clearance of antigen-antibody complexes in the presence of lupus anticoagulant<sup>2,3</sup>. It usually debuts in the form of hemorrhagic events, despite LA positivity<sup>4</sup>. Corticosteroids and other immunosuppressive therapies have been used in its treatment with variable but generally favorable results<sup>5</sup>.

## CASE PRESENTATION

We present the case of a 54-year-old woman diagnosed with Systemic Lupus Erythematosus (SLE) in 1996 with systemic involvement: lupus glomerulonephropathy, cutaneous, serous and joint involvement. Prior to the diagnosis of LAHPS, the patient was serologically positive por ANA, anti-DNA, anti-SSA, anti-Scl70, LA, ACAs and anticardiolipin antibodies (aCL) and was under follow-up by rheumatology in our centre. She had no personal or family history of thrombotic or haemorrhagic events and was on prophylactic antiplatelet treatment with acetylsalicylic acid (ASA) 100mg daily given the triple positivity for antiphospholipid antibodies.

In August 2020, after four days of headache, the patient went to the hospital emergency department where an urgent cranial CT scan was performed showing a left cerebellar haematoma. Antiplatelet therapy was withdrawn at that time, and she progressed favourably without new haemorrhagic complications or secondary neurological sequelae. At that time, she was receiving immunosuppressive treatment with prednisone 5mg daily and cyclosporine 50mg every 12 hours due to her previous diagnosis of SLE. The patient had previously received multiple lines of immunosuppressive treatment as part of the treatment for her previous diagnosis of SLE and had a history of serious adverse events to immunosuppressants, including agranulocytosis secondary to treatment with azathioprine and severe infusional reaction secondary to the administration of rituximab.

The patient was referred to the thrombosis and haemostasis department for a study, which was carried out in October 2020 (Table 1).

On his first evaluation at our clinic, his platelet count was in the normal range, INR 1.44; prothrombin activity (PA) 61%; cephalin time (PTT) 83.1 sec; cephaline mixture test (PTT) 74.9 sec; antigenic fibrinogen 408 mg/dl and Clauss fibrinogen 360 mg/dl. In view of these findings, a study of extrinsic coagulation pathway factors (coagulometric method) was performed and a deficit in FII activity (28%) was observed. Persistent triple positivity for antiphospholipid antibodies was also observed. The study of factors of the intrinsic coagulation pathway with ellagic acid was within the normal range. The study of von Willebrands disease, filling times and platelet aggregations did not show abnormal results.

Given the suspicion of LAHPS, the dose of oral prednisone was increased to 50mg (1mg/kg/day) daily in December 2020, after which FII activity normalised to levels of 68% (Figure 1) in January 2021. A tapering course of corticosteroids was started two weeks after the start of treatment, reaching a dose of 10mg of prednisone daily in March 2021, with a parallel progressive decrease in FII activity to levels of 34%. The patient continued to be monitored by the rheumatology department and in consensus with them, with the aim of starting a decreasing course of corticosteroids until reaching her usual doses, she increased the daily dose of cyclosporine A and associated mycophenolate mofetil with a further increase in the levels of FII to 46% on 10/29/2021. Given the previous adverse effects presented by the patient, it was not possible to use other immunosuppressants commonly used in other cases of LAHPS, such as azathioprine or rituximab.

On 10/29/2021 antiplatelet therapy was reintroduced with ASA 100mg daily. The patient did not present haemorrhagic or thrombotic complications.

### *CONCLUSIONS.*

LAHPS is an uncommon pathology associated with hemorrhagic complications, more common in pediatric age and in young women, with more than half of the patients being under sixteen years of age at diagnosis<sup>1</sup>. Most cases are associated with a diagnosis of SLE or occur secondary to viral infections, the latter especially in pediatric patients, who usually present spontaneous resolution of the picture more often than in cases diagnosed in adulthood<sup>2</sup>. The management, as it has been approached in this case, consists of steroids at high doses of mg/kg/day at the diagnosis of the disease, although there are no established parameters for the treatment of this pathology given the small number of cases described<sup>1</sup>.

The use of immunosuppressants is important for the progressive withdrawal of steroid therapy. Cyclophosphamide is one of the therapeutic options that have been used, either in combination with steroids or in monotherapy with generally favourable results<sup>6,7</sup>. Azathioprine has also been tried in this indication, always in combination with corticosteroids and with variable responses<sup>8,9</sup>. Non-specific intravenous immunoglobulins have been used as an alternative treatment in these patients, with variable responses and always in combination or after previous treatment with steroids<sup>10</sup>. Given the frequent coexistence of LAHPS and SLE in the same patient, in some cases these patients have been treated with hydroxychloroquine, with favorable results in combination with immunoglobulins<sup>11</sup>. Rituximab has been used in some patients, in combination with steroid therapy, especially in pediatric patients, with good response<sup>12,13</sup>. In our case it was not possible to use rituximab or azathioprine given the patient's history of severe adverse drug reactions to these drugs.

Combined treatment in our patient with cyclosporine A, mycophenolate mofetil and corticosteroids has so

far allowed to maintain FII levels in the haemostatic range and to reintroduce antiplatelet therapy with ASA without documenting new haemorrhagic complications to date.

| Test                          | Results                     | Normal range                    |
|-------------------------------|-----------------------------|---------------------------------|
| Platelets                     | 235,000/mm <sup>3</sup>     | 150,000-450,000/mm <sup>3</sup> |
| I.N.R                         | 1.44                        | 0.7-1.3                         |
| Prothrombin activity          | 61%                         | 70-130%                         |
| Cephalin time                 | 83.1 seconds                | 25-38 seconds                   |
| Cephaline mixture test        | 74.9 seconds                |                                 |
| Fibrinogen                    | 408 mg/dl                   | 150-450 mg/dl                   |
| Clauss fibrinogen             | 360 mg/dl                   | 150-400 mg/dl                   |
| Thrombin time                 | 11.7 seconds                | <18 seconds                     |
| Lupus anticoagulant           | Positive                    |                                 |
| PFA-100 Collagen/Epinephrine  | 107 seconds 76 seconds      |                                 |
| Collagen/ADP                  |                             |                                 |
| Fac. VIII                     | 78%                         | 50-150%                         |
| Fact. Von Willebrand: coR     | 263%                        |                                 |
| Fact. Von Willebrand: Ag      | 224%                        |                                 |
| Anticardiolipin AC. ACA (IgG) | Positive 48 GLP 30 MLP      | >20 + >20 +                     |
| ACA (IgM)                     |                             |                                 |
| Ac Antiβ <sub>2</sub> IgG IgM | Positive 284 UI/ml 69 UI/ml | >20 + >20 +                     |
| Fac. IX (ellagic acid)        | 75%                         | 50-150%                         |
| Fac. XI (ellagic acid)        | 89%                         | 50-150%                         |
| Fac. XII (ellagic acid)       | 67%                         | 50-150%                         |
| Fac. II                       | 28%                         | 50-150%                         |
| Fac. V                        | 68%                         | 50-150%                         |
| Fac. VII                      | 95%                         | 50-150%                         |
| Fac. X                        | 68%                         | 50-150%                         |
| Prothrombin time              | 15.6 seconds                | 0,0-13,9 segundos               |
| Fac. II inhibitor             | Not detected                |                                 |
| Fac. II (mixture test)        | 60%                         |                                 |

Table 1. Hemorrhagic diathesis study at diagnosis (October 2020).

*Authorship contribution:*

1. Natalia Acedo ([nataliaacedo@hotmail.com](mailto:nataliaacedo@hotmail.com)): main author, corresponding author. given final approval of the version to be published. Coordination in the drafting process. Responsible for the coagulation laboratory where the study presented in the case was performed.
2. Alejandro Alonso ([aacabrero94@gmail.com](mailto:aacabrero94@gmail.com)): co-author, he was involved in the drafting of the article and revision of the final version.
3. Eliana Samantha Feijóo ([sammyfeijoo@gmail.com](mailto:sammyfeijoo@gmail.com)): co-author, she was involved in the drafting of the article.
4. Cristina García ([garciaherce.cristina@gmail.com](mailto:garciaherce.cristina@gmail.com)): co-author, she was involved in the revisión of the final version.
5. Ana M Ortiz ([lanult@yahoo.es](mailto:lanult@yahoo.es)): co-author, she was involved in the revisión of the final version.
6. Adrián Alegre ([adrian.alegre@telefonica.net](mailto:adrian.alegre@telefonica.net)): co-author, head of haematology department.

The author(s) declare that the research was conducted in accordance with the principles embodied in the Declaration of Helsinki and in accordance with local statutory requirements. All participants gave written informed consent to publication of this article.

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