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CASE REPORT

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Lupus anticoagulant hypoprothrombinemia syndrome: A case report

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Abstract

Lupus anticoagulant hypoprothrombinemia syndrome (LAHPS) is a rare entity associated with an increased risk of hemorrhage. Corticosteroids have been used in its treatment with favorable results. We present the case of a 54-year-old female patient with a personal history of Lupus diagnosed with LAHPS following an episode of cerebellar hemorrhage.

KEYWORDS

anticoagulant, antiphospholipid, hematology, hemorrhage, lupus

1 | 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).[1] 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 LA.[2,3] It usually debuts in the form of hemorrhagic events, despite LA positivity.[4] Corticosteroids and other immunosuppressive therapies have been used in its treatment with variable but generally favorable results.[5]

2 | 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 for antinuclear-antibodies (ANA), anti-double stranded DNA antibodies (anti-dsDNA), anti-Sjögren's-syndrome-related antigen A antibodies (anti-SSA), anti-topoisomerase I antibodies (anti-Scl70), LA, anti-beta 2 glycoprotein antibodies (B2GP1), and anticardiolipin antibodies (ACL) and was to follow-up with the rheumatology department at our center. She had no personal or family history of thrombotic or hemorrhagic events and was on prophylactic antiplatelet treatment with acetylsalicylic acid (ASA) 100 mg daily given the triple positive for antiphospholipid antibodies.

In August 2020, after 4 days of headache, the patient went to the hospital emergency department where an urgent cranial CT scan was performed showing a left cerebellar haematoma. There was no clinical activity of lupus at the time of diagnosis of cerebral hemorrhage and physical examination, including neurological examination, was normal. Antiplatelet therapy was withdrawn at that time, and she progressed favorably without new hemorrhagic complications or secondary neurological sequelae.

At that time, she was receiving immunosuppressive treatment with prednisone 5 mg daily, quinacrine 50 mg every week, and cyclosporine 50 mg every 12 h 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 hemostasis department for a study, which was carried out in October 2020 (Table 1).

On her first evaluation at our clinic, her platelet count was in the normal range, INR 1.44; prothrombin activity (PA) 61%; cephalin time (PTT) 83.1 s; cephaline mixture test (PTT) 74.9 s; 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.

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

Test	Results	Normal range
Platelets	235,000/mm3	150,000–450,000/mm3
I.N.R.	1.44	0.7–1.3
Prothrombin activity	61%	70%–130%
Cephalin time	83.1 s	25–38 s
Cephaline mixture test	74.9 s	
Fibrinogen	408 mg/dL	150–450 mg/dL
Clauss fibrinogen	360 mg/dL	150–400 mg/dL
Thrombin time	11.7 s	<18 s
LA	Positive	
PFA-100		
Collagen/Epinephrine	107 s	
Collagen/ADP	76 s	
Fac. VIII	78%	50%–150%
von Willebrand Factor: activity	263%	
von Willebrand Factor: antigen	224%	
Anticardiolipin AC	Positive	
ACA (IgG)	48 GLP	>20+
ACA (IgM)	30 MLP	>20+
Ac Antiβ2	Positive	
IgG	284 UI/ml	>20+
IgM	69 UI/ml	>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 s	0.0–13.9 s
Fac. II inhibitor	Not detected	
Fac. II (mixture test)	60%	

Abbreviation: AC, antibody; ACA, anticardiolipin antibodies; Ac. AntiB2, anti beta 2 microglobulin antibodies; Fac, coagulation factor; I.N.R, international normalized ratio; LA, lupus anticoagulant.

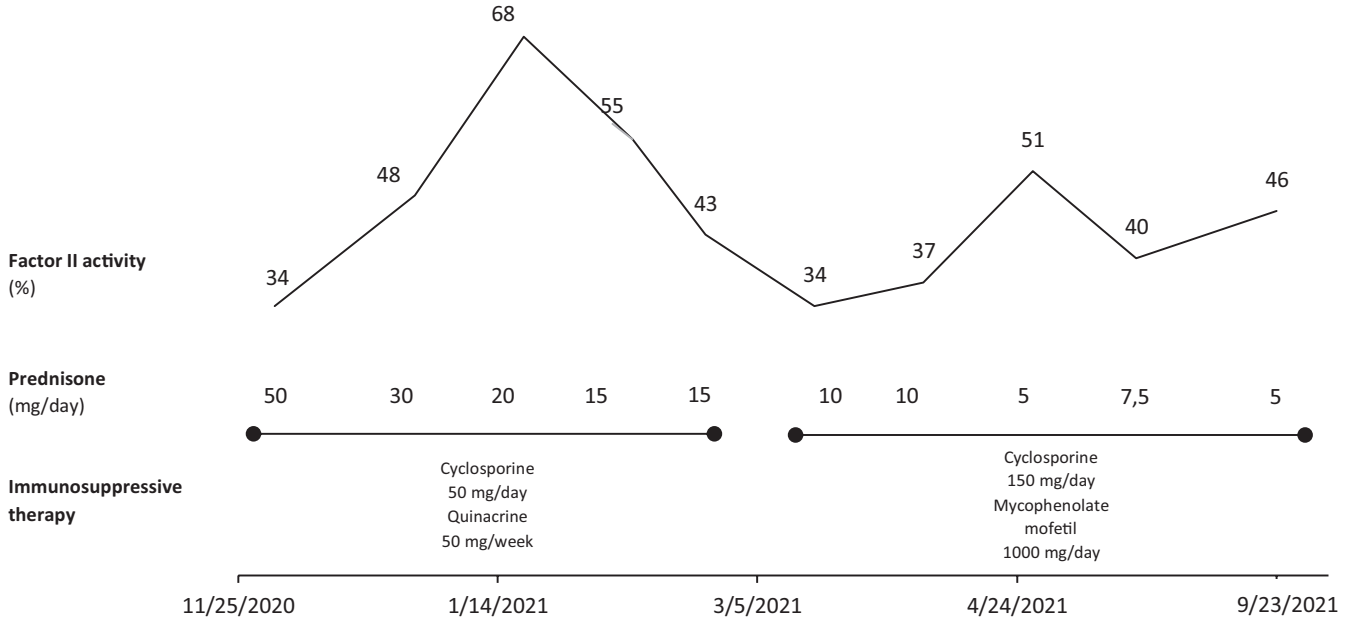

FIGURE 1 Factor II activity evolution throughout treatment.

Given the suspicion of LAHPS, the dose of oral prednisone was increased to 50 mg (1 mg/kg/day) daily in December 2020, after which FII activity normalized to levels of 68% (Figure 1) in January 2021. A tapering course of corticosteroids was started 2 weeks after the start of treatment, reaching a dose of 10 mg 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, they increased the daily dose of cyclosporine A, suspended quinacrine and associated mycophenolate mofetil with a further increase in the levels of FII to 46% in October 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.

In October 2021, antiplatelet therapy was reintroduced with ASA 100 mg daily. The patient did not present hemorrhagic or thrombotic complications.

3 | DISCUSSION

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 16 years of age at diagnosis.[1] 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.[2] 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.[1]

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 favorable results.[6,7] Azathioprine has also been tried in this indication, always in combination with corticosteroids and with variable positivity responses.[8,9] Nonspecific 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.[10] 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.[11] Rituximab has been used in some patients, in combination with steroid therapy, especially in pediatric patients, with a good response.[12,13] 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 hemostatic range and to reintroduce antiplatelet therapy with ASA without documenting new hemorrhagic complications to date.

4 | CONCLUSION

In the present case we have reviewed the most common clinical presentation of LAHPS, in this case in the form of cerebral hemorrhage. Treatment with steroids, together with the association of other immunosuppressants (cyclosporine, mycophenolate mofetil) allowed a progressive reduction of the steroid dose, an increase in FII levels and the absence of new hemorrhagic complications to date.

AUTHOR CONTRIBUTIONS

Natalia Acedo: Project administration; supervision; validation; writing – review and editing. **Alejandro Alonso:** Conceptualization; writing – original draft. **Eliana Samantha Feijoó:** Conceptualization; methodology; visualization. **Cristina García:** Methodology; supervision; validation. **Ana M Ortiz:** Investigation; resources. **Adrián Alegre:** Project administration; supervision; validation.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

Data available within the article or its supplementary materials.

CONSENT

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy

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