Severe ADAMTS13 deficit with a thrombotic thrombocytopenic purpura in a case of inaugural systemic lupus erythematosus with antiphospholipid syndrome

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Summary

ADAMTS13, an important enzyme in the regulation of von Willebrand factor, may be deficient, leading to a thrombotic thrombocytopenic purpura, a subtype of thrombotic microangiopathy causing thrombocytopenia, organ failure and haemolytic anaemia. This condition may also be associated with antiphospholipid syndrome and / or systemic lupus erythematosus. We report a case of ischaemic neurological lesions due to an inaugural systemic lupus erythematosus and antiphospholipid syndrome, with the demonstration of a decreased ADAMTS13 activity without biological signs of thrombotic microangiopathy, associated with a possible COVID-19 trigger.

Key messages for Clinical Practice

1. The diagnosis of thrombotic microangiopathy (which includes HUS and TTP) is based on the triad: mechanical hemolytic anemia, thrombocytopenia, and organ failure.
2. TTP is characterized by a reduction in ADAMTS13, which can be acquired or congenital, leading to the accumulation of vWF multimers in the plasma. The PLASMIC score exists to help guide the diagnosis.
3. Antiphospholipid antibody syndrome is an autoimmune disease linked to the IgG and/or IgM isotypes of anticardiolipin antibodies, anti-beta2-glycoprotein I antibodies, and lupus anticoagulant. It is characterized by thrombotic states and moderate thrombocytopenia. Treatment is based on anticoagulation and immunosuppressants.

Introduction

Thrombotic thrombocytopenic purpura is part of the thrombotic microangiopathies along with the hemolytic uremic syndrome. It is characterized by hemolytic anemia, thrombocytopenia, and organ failure (with frequent cerebral involvement). It can be congenital or acquired, for example, in the course of hematopoietic stem cell transplantation, systemic diseases (such as

systemic lupus erythematosus), or exposure to toxins. It is caused by a reduction in ADAMTS13, the enzyme involved in regulating von Willebrand factor.
Antiphospholipid antibody syndrome is an autoimmune disease linked to the presence of anticardiolipin antibodies, anti-beta2-glycoprotein I antibodies, and lupus anticoagulant. It is also characterized by a prothrombotic state and thrombocytopenia. We report a case of ischemic neurological lesions due to inaugural systemic lupus erythematosus and antiphospholipid syndrome, with the demonstration of decreased ADAMTS13 activity without biological signs of thrombotic microangiopathy, associated with a possible COVID-19 trigger.

Case Report

We report the case of a 47-year-old patient admitted in April 2023 in another hospital for a bilateral visual impairment and headaches. His medical history is marked by arterial hypertension and active smoking (25 pack-year), but also notably an *a frigore* peripheral facial palsy 10 years prior his admission and excessive photosensitivity with the occurrence of erythematous plaques. A brain magnetic resonance imaging (MRI) was conducted, which led to the discovery of an acute ischemic lesion of the right occipital lobe. The neurovascular assessment consisted of transoesophageal echocardiogram, conventional Holter monitoring and general blood biology. The only noticeable anomaly was a thrombopenia and an elevation of the 8th coagulation factor (FVIII). He was discharged from the hospital with an idiopathic origin of the stroke and on Acetylsalicylic acid.

The patient was then referred to the Neurology Department in July 2023 by an Ophthalmologist in our hospital after the discovery of a left inferior homonymous lateral quadrantanopia, due to a worsening of the visual symptoms. The thorough clinical examination did not show any other neurological abnormalities, but *livedo reticularis* was highlighted. A brain MRI was performed, showing many new ischaemic lesions in the supra- and infra-tentorial regions. Due to the recurring and unexplained neurological manifestations (stroke events), the initial assessment was completed by the exploration of the thrombocytopenia, which was still present. A splenomegaly was ruled out by an abdominal ultrasound and there was no drug toxicity. The haematologists recommended further laboratory investigations to exclude a thrombotic microangiopathy (TMA).

The patient's biological results were the following: Acid citrate dextrose (ACD) platelets 42.000/mm^3 with 10% Immature Platelet Fraction (IPF); no schistocytes; normal reticulocytes count; haptoglobin at 0,33 g/L; Activated Partial Thromboplastin Time (APTT) at 94 seconds; normal fibrinogen level; lactate dehydrogenase (LDH) level at 263 U/L; normal bilirubin levels. The complement was within normal range (C3 at 118 mg/dL and C4 at 23 mg/dL). These results could not highlight a significant haemolysis (absence of schistocytes, noregenerative anaemia, etc). Further laboratory investigations were performed: negative flow cytometric detection of PNH clones (Paroxysmal Nocturnal Haemoglobinuria), negative anti-cardiolipin and anti-beta2 glycoprotein I IgG antibodies. The laboratory data confirmed the diagnosis of Lupus Anticoagulant (LA) positivity, included extended APTT clotting time by 94 sec (ref 28-43 sec); Rosner index (mixing test) increased at 29,7% (cut-off value <12%); a positive screen dRVVT test at 62.9 sec (ref <45.8) with a positive confirm dRVVT test at 31,4 sec (ref <40,9) and a normalised ratio of 2 (cut-off value <1.2); anti-dsDNA at 244.3 mUI/L (ref <27); speckled anti-nuclear antibodies at 640 (ref <80); anti-nucleosome and anti SSB antibodies positive; a low rate of protease ADAMTS13 activity at 0,2 (ref 69-144) with elevation of anti-ADAMTS13 antibodies at 83,872 U/mL (ref <13 U/ml). The anti-PR3 and anti-MPO antibodies were negative. These finding correlate with a diagnosis of SLE and antiphospholipid syndrome (APS), with the particularity of anti-ADAMTS13 antibodies without TMA.

Discussion

The diagnosis of TMA, including thrombotic thrombocytopenic purpura (TTP) and haemolytic uremic syndrome (HUS), is based on the following triad: mechanical haemolytic anaemia (negative Coombs test, presence of schistocytes), thrombocytopenia and organ failure. TMA can also occur in other conditions like neoplasm, HIV infection, heparin-induced thrombocytopenia, HELLP (Haemolysis, Elevated Liver enzymes and Low Platelets) syndrome, haematopoietic cell transplantation, toxics, systemic lupus erythematosus (SLE), etc.[1–3] TTP is a haematological disorder characterised by thrombocytopenia, microangiopathic haemolytic anaemia and organ disorders. It is linked to innate or acquired activity (< 10%) of the enzyme disintegrin and metalloprotease with thrombospondin type I repeats-13 (ADAMTS13), leading to an increased platelet aggregation.[4] Indeed, the role of ADAMTS13 is to regulate the size of von Willebrand factor (vWF) multimers. In case of functional deficit of the enzyme, there is an accumulation of large-sized vWF multimers in the plasma leading to

spontaneous formation of microthrombi in the microcirculation.[5] The incidence of acquired TTP is approximately 4 cases per million inhabitants per year.[6] We distinguish an acquired form and a congenital form, the latter consisting of heterozygous or homozygous mutations of a component of ADAMTS13 (Upshaw-Schulman Syndrome). The hereditary form occurs in children (homozygous mutation) or around the twenties (heterozygous mutation).[7] The thrombotic manifestations are mainly cerebral in the TTP (60% of patients) and vary clinically from paraesthesia to coma.[8] The diagnosis is mainly based on blood analysis: blood smear, renal function, coagulation panel, liver function tests, measurement of ADAMTS13 activity and autoantibodies anti-ADAMTS13. The PLASMIC score or French score can help guide towards a diagnosis of TTP (table 1). It is also important to search for associated secondary aetiology through stool analysis (differential diagnosis with HUS), serology (HIV), complement and autoimmune panel.[9]

SLE corresponds to abnormal production of antibodies directed against components of apoptotic cellular bodies. Autoimmune response is exacerbated by excessive cytokine and chemokine production as well as heightened B and T lymphocyte activity. As a systemic disease, its main clinical manifestations include arthralgia and arthritis (80% of cases), fever, skin rash, lymphadenopathy, cytopenia, respiratory complaints (pleural effusion, lupus pneumonitis), cardiac involvement (pericarditis, myocarditis, Libman-Sacks endocarditis), neurological issues (stroke, seizures, etc), hypertension, Raynaud's syndrome, and more. The incidence is estimated at 3-4 per 100000 inhabitants per year in France. The diagnosis primarily relies on comprehensive laboratory analysis, including a full autoimmune panel (antinuclear antibodies ANA, anti-DNA antibodies, ENA antibodies, anti-phospholipid antibodies), as well as CH50 complement and C3-C4 fractions measurements. Additionally, testing C-reactive protein, erythrocyte sedimentation rate, fibrinogen, serum protein electrophoresis, serum creatinine, and screening for proteinuria is recommended. In case of renal involvement suggested by laboratory findings, a complete urinary examination (24-hour urine collection, renal biopsy if proteinuria > 5g/g f creatinine) should be conducted.[10,11]

APS is an autoimmune disease linked to IgG and/or IgM isotypes of the anticardiolipin (aCL) antibodies, anti-β2 glycoprotein I (aβ2GPI) antibodies, and/or the lupus anticoagulant (LA), found at least twice after 12 weeks in the blood testing. It leads to thrombosis and is often revealed by cerebrovascular diseases. However, there are many other neurological manifestations, such as chorea, dementia, epilepsy, etc. Since 2023, there is a new and better

classification criteria for APS (table 3). The mechanisms leading to thrombosis are not yet fully understood but an increase in the expression of procoagulant and proinflammatory molecules have been described.[12] Thrombocytopenia is described in 20 to 50% cases and is thought to be linked to platelet consumption by the antibodies. It is correlated to a higher severity of the disease due to more thrombotic complications, such as cutaneous or musculoskeletal manifestations, neurological events, and the use of immunosuppressive treatments.[13,14] In our patient's case, the recurrence of ischaemic lesions and livedo reticularis, correlated with a thrombocytopenia and LA positivity, highlights the diversity of APS. Indeed, there are various clinical phenotypes as some APS are associated with SLE and/or other manifestations (thrombocytopenia, livedo reticularis, cognitive impairment, etc).[15,16]

An interesting serological finding in this patient is the positivity of SARS-CoV-2 anti-nucleocapsid Ig. Some authors have reported cases of acquired autoimmune TTP, APS or autoimmune haemolytic anaemia associated with COVID-19. In this case, there is a possibility of an immune trigger leading to the development of SLE with APS.[17–20]

After the demonstration of SLE with APS, the patient was treated with a 4-day course of Dexamethasone 40 mg corticosteroid therapy during the hospitalisation, along with an anticoagulant (low molecular weight heparin, followed by vitamin K antagonist - VKA). Hydroxychloroquine 200 mg 2 tablets once a day was prescribed after improvement of thrombocytopenia. Upon receiving the first ADAMTS13 result, Rituximab was initiated after multidisciplinary consultation, despite the absence of clear signs of TTP on biological tests (especially schistocytes). A serie of four weekly courses of Rituximab 375 mg/m^2 were initiated to lower the patient's anti-ADAMTS13 antibody levels. The combination of treatments (Rituximab, Plaquenil) led to a reduction in the anti-ADAMTS13 antibody levels and the absence of any other lupus signs. The patient had a clinical improvement namely of his vision two months after the second stroke. He has resumed his activities after the 4 courses of Rituximab. The protease ADAMTS13 activity increased at 39,2% after two courses of Rituximab and normalised 78,6% after the four courses (figure 1). Platelets levels have normalised. The titre of anti-DNA antibodies decreased significatively after 6 months (figure 2) and the LA positivity disappeared after 9 months. Follow-up is based on ADAMTS13 levels, anti-DNA levels and clinical signs. Rituximab treatment could be resumed in case of relapse.

The treatment of lupus with APS will depend on the clinical and laboratory suspicion of TTP. In case of high suspicion, plasma exchanges (1-1,5 plasma volume per day until platelet count above 150000/mm³ for 48 hours) and corticosteroids therapy (Methylprednisolone then Prednisolone at 1 to 1,5 mg/kg/day for 3 weeks followed by a gradual dose reduction regime) combined with folate supplementation should be administered before the ADAMTS13 assay results are available. The administration of Caplacizumab will depend on its availability and can be started before ADAMTS13 results. However, a result > 20% leads to an interruption of the treatment and a reconsideration of the diagnosis. Rituximab treatment (4 perfusions of 375 mg/m^2 once a week) would be initiated if the result is < 10% to reduce the levels of ADAMTS13 autoantibodies. If the ADAMTS13 assay is not available within 7 days, Caplacizumab is not recommended on the opposite of Rituximab, in combination with plasma exchange and corticosteroid therapy. Regarding the patients with intermediate or low suspicion of TTP, the decision to use plasma exchanges and corticosteroid therapy needs to be made by the clinician. Initiation of Rituximab or Caplacizumab treatment should only occur after receiving the results of ADAMTS13 and anti-ADAMTS13 IgG.[1,21,22] It is recommended to initiate prophylactic anticoagulation in all patients in the acute phase of TTP as soon as the platelet count is above 50000/mm³. The treatment of the TTP should be administered as quickly as possible, with a survival rate of 80-90%.[23] In the case of SLE-APS, a treatment by Hydroxychloroquine should be administered as maintenance treatment even in the absence of thrombotic history, and low dose of aspirin is recommended (thromboprotective effect).[24] The mortality rate is high in the absence of treatment (> 90%) and decreases to 10-30% after treatment. The rate of relapse and refractory TTP is high (40%), underscoring the importance of regular follow-up.[25] When thrombocytopenia is associated with APS and thrombotic complications, extended anticoagulation with VKAs (target INR between 2-3) is considered. Splenectomy is reserved in refractory cases.[11,16] Finally, the treatment of SLE without APS and TMA depends on the renal involvement and the severity of the condition (table 2).

Conclusion

In conclusion, we discussed the case of a patient with the onset of neurological and cutaneous manifestations leading to the demonstration of the association of systemic lupus erythematosus and antiphospholipid syndrome, associated with a thrombocytopenia. It highlights the importance to identify TTP as promptly as possible by measuring ADAMTS13 levels and anti-ADAMTS13 antibodies. However, if clinical and laboratory criteria strongly suggest TTP, waiting for results should not delay the initiation of plasma exchanges and

corticosteroid therapy. In the case of our patient, it was important to initiate anticoagulant treatment to prevent any recurrence of stroke as well as worsening of the existing neurological disorders. Nevertheless, due to a low ADAMTS13 activity, the rapid initiation of Rituximab, combined with hydroxychloroquine, played probably a key role in preventing the occurrence of TMA and in favourable serological and clinical evolution of the lupus with APL syndrome of this patient.

Table 1

PLASMIC score or French score (reprinted from [26] with permission from Elsevier).

Parameters	French Score	PLASMIC Score
Platelet count	<30 × 10^9/L (+1)	<30 × 10^9/L (+1)
Serum creatinine level	<2.26 mg/dL (+1)	<2.0 mg/dL (+1)
Hemolysis Indirect bilirubin >2 mg/dL or reticulocyte count >2.5% or undetectable haptoglobin	[a]	+1
No active cancer in previous year	[a]	+1
No history of solid organ or SCT	[a]	+1
INR < 1.5	[a]	+1
MCV < 90 fL	NA	+1
Likelihood of severe deficiency of ADAMTS13 activity (<10%)	0: 2%	0-4: 0%-4%
	1: 70%	5: 5%-24%
	2: 94%	6-7: 62%-82%

Note: Each item is associated with 1 point (+1). The table is adapted from Joly BS.[53]

Abbreviations: INR, international normalized ratio; MCV, mean corpuscular value; SCT, stem cell transplantation.

[a]French score considered patients with thrombotic microangiopathy

Table 2

EULAR recommendations (update 2023) for the management of systemic lupus erythematosus (reprinted from [27] with permission from BMJ).

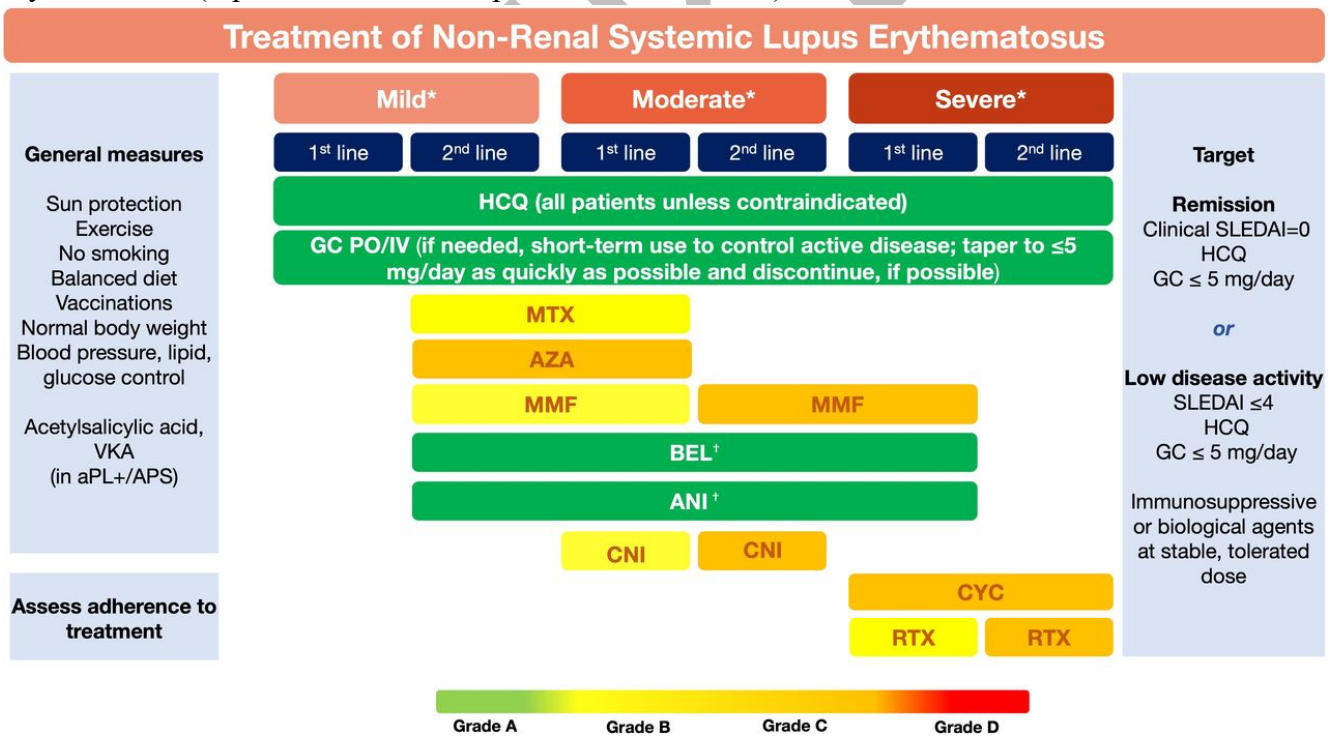


Table 3

Definitions of the 2023 ACR/EULAR antiphospholipid syndrome classification criteria (reprinted from [28] with permission from BMJ).

Entry Criteria[a]

At least one documented[b] clinical criterion listed below (domains 1-6)

plus

A positive antiphospholipid antibody (aPL) test

(a lupus anticoagulant test, or moderate-to-high titers of anticardiolipin or anti-β_2-glycoprotein-I antibodies [IgG or IgM])

within three years[b] of the clinical criterion

If absent, do not attempt to classify as APS - If present, apply additive criteria

Additive clinical and laboratory criteria[a]

Do not count a clinical criterion if there is an equally or more likely explanation than APS.

Within each domain, only count the highest weighted criterion towards the total score.

Clinical domains and criteria	Weight		Weight
D1. Macrovascular (Venous Thromboembolism [VTE])		**D2. Macrovascular (Arterial Thrombosis [AT])**	
VTE with a high-risk VTE profile[c]	1	AT with a high-risk CVD profile[c]	2
VTE without a high-risk VTE profile[c]	3	AT without a high-risk CVD profile[c]	4
D3. Microvascular		**D4. Obstetric**	
Suspected (one or more of the following)	2	≥3 Consecutive pre-fetal (<10w) and/or early fetal (10w 0d -15w 6d) deaths	1
Livedo racemosa (exam)			
Livedoid vasculopathy lesions (exam)			
Acute/chronic aPL-nephropathy (exam or lab)			
Pulmonary hemorrhage (symptoms and imaging)		Fetal death (16w 0d – 33w 6d) in the absence of pre-eclampsia (PEC) with severe features or placental insufficiency (PI) with severe features	1
Established (one of more of the following)	5		
Livedoid vasculopathy (pathology[d])			
Acute/chronic aPL-nephropathy (pathology[d])		PEC with severe features (<34w 0d) or PI with severe features (<34w 0d) with/without fetal death	3
Pulmonary hemorrhage (BAL or pathology[d])			
Myocardial disease (imaging or pathology)		PEC with severe features (<34w 0d) and PI with severe features (<34w 0d) with/without fetal death	4
Adrenal hemorrhage (imaging or pathology)			
D5. Cardiac Valve		**D6. Hematology**	
Thickening	2	Thrombocytopenia (lowest 20-130x10^9/L)	2
Vegetation	4		
Laboratory (aPL) domains and criteria[e]	**Weight**		
D7. aPL test by coagulation-based functional assay (lupus anticoagulant test [LAC])		**D8. aPL test by solid phase assay (anti-cardiolipin antibody [aCL] ELISA and/or anti-β_2-glycoprotein-I antibody [aβ_2GPI] ELISA [persistent])**	
Positive LAC (single – one time)	1	Moderate or high positive (IgM) (aCL and/or aβ_2GPI)	1
Positive LAC (persistent)	5	Moderate positive (IgG) (aCL and/or aβ_2GPI)	4
		High positive (IgG) (aCL or aβ_2GPI)	5
		High positive (IgG) (aCL and aβ_2GPI)	7

TOTAL SCORE

Classify as Antiphospholipid Syndrome for research purposes if there are at least 3 points from clinical domains AND at least 3 points from laboratory domains

Figure 1

The patient's biological ADAMTS13 activity before and after the initiation of Rituximab (4 courses)

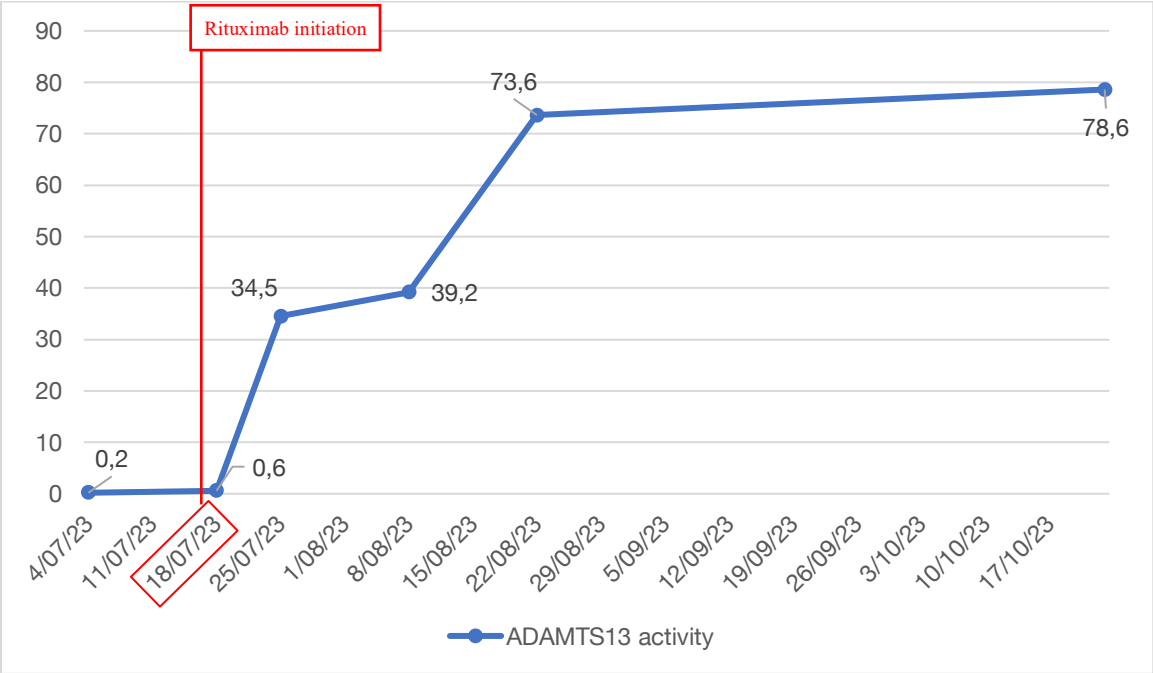
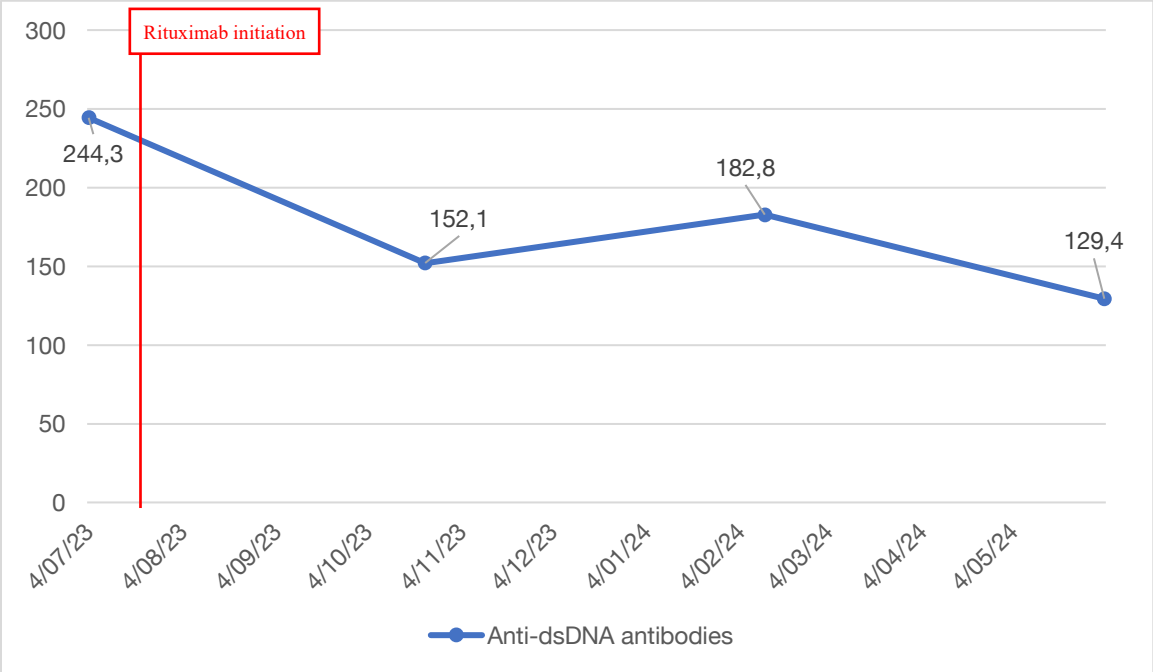


Figure 2

The patient's biological anti-dsDNA antibody titre before and after the treatment



References

1. Coppo P, Veyradier A. Microangiopathies thrombotiques : physiopathologie, diagnostic et traitement. Réanimation. 2005 Nov;14(7):594–603.
2. Yue C, Su J, Gao R, et al. Characteristics and Outcomes of Patients with Systemic Lupus Erythematosus–associated Thrombotic Microangiopathy, and Their Acquired ADAMTS13 Inhibitor Profiles. J Rheumatol. 2018 Nov;45(11):1549–56.
3. Yue C, Su J, Fan X, et al. Immune-mediated thrombotic thrombocytopenic purpura in patients with and without systemic lupus erythematosus: a retrospective study. Orphanet J Rare Dis. 2020 Aug 28;15(1):225.
4. Sukumar S, Lämmle B, Cataland SR. Thrombotic Thrombocytopenic Purpura: Pathophysiology, Diagnosis, and Management. J Clin Med. 2021 Feb 2;10(3).
5. Garcia Boyero R, Mas Esteve E, Mas Esteve M, et al. Systemic lupus erythematosus and thrombotic thrombocytopenia purpura: a refractory case without lupus activity. Reumatol Clin. 2013;9(6):373–5.
6. Mariotte E, Azoulay E, Galicier L, et al. Epidemiology and pathophysiology of adulthood-onset thrombotic microangiopathy with severe ADAMTS13 deficiency (thrombotic thrombocytopenic purpura): a cross-sectional analysis of the French national registry for thrombotic microangiopathy. Lancet Haematol. 2016 May;3(5):e237-45.
7. Borborema TS, Diniz SSL, Lima J de S, et al. Hereditary thrombotic thrombocytopenic purpura: a case report. Hematol Transfus Cell Ther. 2022;44(2):269–71.
8. Scully M, Yarranton H, Liesner R, et al. Regional UK TTP registry: correlation with laboratory ADAMTS 13 analysis and clinical features. Br J Haematol. 2008 Sep;142(5):819–26.
9. Adler M, Kremer Hovinga JA, Lämmle B. [Thrombotic thrombocytopenic purpura--an often missed diagnosis]. Rev Med Suisse. 2014 Nov 26;10(452):2280–4.
10. Couture P, Hie M, Pineton De Chambrun M, et al. Caractéristiques cliniques, pronostiques et traitement des syndromes de microangiopathie thrombotique au cours du lupus : une étude descriptive multicentrique. Rev Med Interne. 2017 Jun;38:A107–8.
11. Almoura Z, Antignac M, Bader-Meunier B, et al. Protocole National de Diagnostic et de Soins (PNDS) [Internet]. HAS Santé. 2017 [cited 2023 Nov 2]. Available from: https://www.has-sante.fr/upload/docs/application/pdf/2017-03/dir1/pnds_-_lupus_systemique.pdf
12. Man YL, Sanna G. Neuropsychiatric Manifestations of Antiphospholipid Syndrome—A Narrative Review. Brain Sci. 2022 Jan 11;12(1):91.
13. Gamal S, Mohamed S, Moghazy A. Thrombocytopenia in a cohort of primary and secondary antiphospholipid syndrome patients: Relation to clinical, laboratory manifestations and damage index. Arch Rheumatol. 2022 Jun 1;37(2):252–60.
14. Artim-Esen B, Diz-Küçükkaya R, İnanç M. The significance and management of thrombocytopenia in antiphospholipid syndrome. Curr Rheumatol Rep. 2015 Mar;17(3):14.
15. Qi W, Zhao J, Huang C, et al. Clinical characteristics and prognosis of patients with antiphospholipid antibodies based on cluster analysis: an 8-year cohort study. Arthritis Res Ther. 2022 Dec 11;24(1):140.
16. Vreede AP, Bockenstedt PL, McCune WJ, et al. Cryptic conspirators: a conversation about thrombocytopenia and antiphospholipid syndrome. Curr Opin Rheumatol. 2019 May;31(3):231–40.

17. Kornowski Cohen M, Sheena L, Shafir Y, et al. An Early Unexpected Immune Thrombotic Thrombocytopenic Purpura Relapse Associated with SARS-CoV-2 Infection: A Case Report and Literature Review. Acta Haematol. 2021;144(6):678–82.
18. Hindilerden F, Yonal-Hindilerden I, Akar E, et al. Covid-19 associated autoimmune thrombotic thrombocytopenic purpura: Report of a case. Thromb Res. 2020 Nov;195:136–8.
19. Zhang Y, Xiao M, Zhang S, et al. Coagulopathy and Antiphospholipid Antibodies in Patients with Covid-19. New England Journal of Medicine. 2020 Apr 23;382(17).
20. Lopez C, Kim J, Pandey A, et al. Simultaneous onset of COVID-19 and autoimmune haemolytic anaemia. Br J Haematol. 2020 Jul 22;190(1):31–2.
21. Zheng XL, Vesely SK, Cataland SR, et al. ISTH guidelines for the diagnosis of thrombotic thrombocytopenic purpura. J Thromb Haemost. 2020 Oct;18(10):2486–95.
22. Alwan F, Vendramin C, Vanhoorelbeke K, et al. Presenting ADAMTS13 antibody and antigen levels predict prognosis in immune-mediated thrombotic thrombocytopenic purpura. Blood. 2017 Jul 27;130(4):466–71.
23. Gavriilaki E, Nikolousis E, Koravou EE, et al. Caplacizumab for immune thrombotic thrombocytopenic purpura: real-world multicenter data. Front Med (Lausanne). 2023;10:1226114.
24. Fayyaz A, Igoe A, Kurien BT, et al. Haematological manifestations of lupus. Lupus Sci Med. 2015;2(1):e000078.
25. Zalazar P, Coral I. Thrombotic Thrombocytopenic Purpura as The Debut of Systemic Lupus Erythematosus. Pollution and Effects on Community Health. 2023 Apr 14;2(2).
26. Zheng XL, Vesely SK, Cataland SR, et al. ISTH guidelines for the diagnosis of thrombotic thrombocytopenic purpura. Journal of Thrombosis and Haemostasis. 2020 Oct;18(10):2486–95.
27. Fanouriakis A, Kostopoulou M, Andersen J, et al. EULAR recommendations for the management of systemic lupus erythematosus: 2023 update. Ann Rheum Dis. 2024 Jan;83(1):15–29.
28. Barbhaiya M, Zuily S, Naden R, et al. 2023 ACR/EULAR antiphospholipid syndrome classification criteria. Ann Rheum Dis. 2023 Oct;82(10):1258–70.