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Catastrophic antiphospholipid syndrome in a patient with severe and refractory immune thrombocytopenic purpura: A case report

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ABSTRACT

Background: Catastrophic Antiphospholipid Syndrome (CAPS) is a rare but life-threatening manifestation of Antiphospholipid Syndrome (APS), characterized by rapidly progressive multi-organ thrombosis and a mortality rate exceeding 40%. Its coexistence with refractory Immune Thrombocytopenic Purpura (ITP) creates an exceptionally complex clinical scenario defined by simultaneous hemorrhagic and thrombotic risks, with management directed at correcting thrombocytopenia to permit safe anticoagulation while implementing preventive antithrombotic measures during the interim period.

Case Presentation: We report a case of severe refractory ITP in a 39-year-old female with confirmed APS who subsequently developed a CAPS event involving peripheral, pulmonary, and central vascular territories, despite multiple lines of escalating immunosuppressive therapy, thrombopoietin receptor agonist use, and splenic embolization.

Discussion: Management requires the simultaneous pursuit of two clinical imperatives: correcting platelet counts to permit safe anticoagulation and implementing antithrombotic

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prophylaxis during the interval in which anticoagulation cannot be safely instituted. Treatment of thrombocytopenia escalates through corticosteroids and intravenous immunoglobulin (IVIG) as first-line agents, followed by immunosuppressants and thrombopoietin receptor agonists (TPO-RAs) as second-line options; procedural interventions are reserved for refractory cases. In catastrophic situations, combined therapy comprising full anticoagulation (whenever feasible), pulse corticosteroid therapy, and plasmapheresis and/or IVIG constitutes the standard of care. Importantly, TPO-RAs carry a recognized thrombotic risk in patients with pre-existing hypercoagulable states, as demonstrated in this case.

Conclusion: The CAPS/refractory ITP association illustrates the boundaries of current therapeutic strategies. Even with aggressive, multidisciplinary, and coordinated interventions, clinical response may remain limited, reinforcing the need for novel therapeutic approaches to this complex autoimmune condition.

Keywords: *antiphospholipid syndrome; catastrophic antiphospholipid syndrome; immune thrombocytopenic purpura; refractory thrombocytopenia; eltrombopag.*

1. INTRODUCTION

Catastrophic Antiphospholipid Syndrome (CAPS) is a rare, acute, and fulminant form of Antiphospholipid Syndrome (APS), defined by rapidly progressive disseminated thromboses involving at least three organ systems, with an overall mortality exceeding 40% despite therapeutic advances [1,2,3]. The simultaneous presence of Immune Thrombocytopenic Purpura (ITP) causing severe and refractory thrombocytopenia constitutes an extremely complex clinical scenario, demanding rapid diagnosis, adequate risk stratification, and aggressive multidisciplinary management.

In general, treatment goals encompass symptom control, correction of platelet counts to values permitting safe anticoagulation (>50,000/mm³), and prevention of thromboembolic events during the interval in which anticoagulation cannot be instituted [4,5].

First-line treatment consists of corticosteroids; in cases of non-response, symptom worsening, or intolerance to adverse effects, immunosuppressants such as cyclophosphamide (CYC), azathioprine (AZA), mycophenolate mofetil (MMF), or rituximab (RTX) are indicated. Hydroxychloroquine (HCQ) may provide antithrombotic protection, particularly in APS associated with systemic lupus erythematosus (SLE) [6,7]. When rapid platelet recovery is required, intravenous immunoglobulin (IVIG) in conjunction with corticosteroid therapy is indicated [4,8]. Thrombopoietin receptor agonists (TPO-RAs), notably eltrombopag, are also available to stimulate platelet production and reduce bleeding risk [9,10].

2. CASE REPORT

A 39-year-old female patient presented with an episode of deep vein thrombosis (DVT) without identifiable risk factors, accompanied by anemia, thrombocytopenia, and persistently elevated titers of lupus anticoagulant, anti-cardiolipin IgG, and anti-cardiolipin IgM antibodies on repeated testing, fulfilling the ACR/EULAR 2023 classification criteria for APS. Due to severe thrombocytopenia (20,000/mm³), anticoagulation could not be initiated; the patient was started on hydroxychloroquine and full-dose azathioprine, with no clinical response. She subsequently developed worsening thrombocytopenia, petechiae, and active bleeding (epistaxis and gingival hemorrhage).

Intravenous immunoglobulin (IVIG) was administered with minimal response, and platelets dropped below 6,000/mm³ within one week of infusion. Thereafter, pulse therapy with methylprednisolone and dexamethasone was performed, along with repeated IVIG cycles, with persistently critical platelet values and ongoing bleeding episodes. Plasmapheresis could not be performed due to the severity of thrombocytopenia and limited procedural access. Given the refractory nature of the condition, immunosuppression with rituximab was initiated but subsequently discontinued due to lack of adequate response.

Due to persistent refractoriness, a multidisciplinary discussion with Hematology was conducted, and bortezomib was introduced but discontinued following an infectious complication (*Pneumocystis jirovecii* pneumonia). Shortly after withdrawal of immunosuppressants, genitourinary tuberculosis was also diagnosed.

Bone marrow aspiration performed for differential diagnosis and exclusion of primary hematological diseases revealed hypoplasia of the megakaryocytic lineage. Eltrombopag was therefore initiated and progressively titrated to the maximum approved dose (75 mg/day). However, one month after treatment initiation, the patient developed a CAPS event involving peripheral, pulmonary, and central vascular territories (DVT of the right lower limb, pulmonary embolism, and ischemic stroke). Urgent combined therapy with pulse methylprednisolone and IVIG was instituted, and an inferior vena cava (IVC) filter was placed due to absolute contraindication to anticoagulation.

Following clinical stabilization, splenic embolization (SE) was performed in conjunction with low-dose eltrombopag (25 mg/day). Neither intervention achieved satisfactory platelet recovery, with counts remaining at 2,000/mm³. Given the absence of response to embolization, splenectomy was considered but ultimately not performed.

3. DISCUSSION

The coexistence of ITP and APS/CAPS represents the quintessential therapeutic paradox in autoimmune medicine: concurrent hemorrhagic and thrombotic risks with a profound impact on patient survival [2,4]. The present case illustrates the critical challenge faced by rheumatologists when full anticoagulation is contraindicated by bleeding risk, while its absence perpetuates thrombotic catastrophe [1,2]. The severity and refractoriness of the autoimmune process, combined with recurrent infectious complications arising from prolonged immunosuppression, rendered standard therapeutic protocols largely ineffective and limited the use of combined CAPS therapy at critical junctures.

The therapeutic strategy must simultaneously address two distinct clinical imperatives: correcting platelet counts to above 50,000/mm³ to enable safe anticoagulation, and implementing antithrombotic prophylaxis during the interval in which anticoagulation cannot be safely instituted [4,5].

Management of thrombocytopenia begins with discontinuation of anticoagulation and, in cases of active bleeding, appropriate hemostatic control. First-line therapy consists of corticosteroids, with methylprednisolone or dexamethasone pulse therapy indicated in severe cases [4,5]. IVIG may be added in refractory autoimmune thrombocytopenia with severe bleeding [4,8]. Steroid-sparing immunosuppressants (AZA, MMF, and CYC) constitute second-line therapeutic options [4].

Rituximab is an effective option in corticosteroid-refractory ITP or following relapse after initial therapies [5,11]. Its mechanism involves depletion of circulating B lymphocytes via complement-dependent cytotoxicity, antibody-dependent cellular cytotoxicity, and direct apoptosis [11]. In ITP, the reduction of B cells decreases anti-platelet autoantibody production and modulates antigen presentation and T-helper cell activation, thereby contributing to platelet recovery [11].

Thrombopoietin receptor agonists (TPO-RAs) have demonstrated utility in both refractory ITP and aplastic anemia [9,10]. In refractory ITP, eltrombopag consistently elevates platelet counts in a sustained manner and reduces hemorrhagic episodes. Beyond megakaryocyte stimulation, evidence suggests that eltrombopag may exert indirect immunomodulatory effects, contributing to decreased platelet destruction [9]. In aplastic anemia, its mechanism extends beyond megakaryocytic stimulation; studies have demonstrated multilineage responses — including increments in hemoglobin, neutrophils, and platelets — suggesting potential activity at earlier hematopoietic progenitors and promoting global hematopoietic recovery.

Importantly, there is an inherent paradox in the use of TPO-RAs in the context of APS/CAPS: these agents carry a recognized thrombotic risk, particularly in patients with pre-existing hypercoagulable states [9,10]. This risk is directly illustrated in the present case, in which the CAPS event occurred one month after eltrombopag initiation, a temporal association consistent with previously reported cases [12,13].

Antithrombotic prophylaxis during the period when anticoagulation is not feasible is essential. HCQ demonstrably reduces thrombotic risk, particularly in APS associated with SLE [6,7]. Low-dose aspirin is permissible when platelets exceed 30,000/mm³ and active bleeding has resolved. Once the platelet count surpasses 50,000/mm³ without active bleeding, anticoagulation should be reinitiated, preferably with low-molecular-weight heparin (LMWH) with subsequent transition to vitamin K antagonists (VKA) [7]. In patients with previous severe arterial events, the addition of aspirin after clinical stabilization should be considered. Non-pharmacological measures — including intermittent pneumatic compression, elastic compression stockings, and early ambulation — are likewise important. Inferior vena cava filter placement may be considered in cases of recurrent venous thrombosis with absolute contraindication to anticoagulation, although it does not prevent arterial events and remains a subject of clinical debate [14]. These management strategies are summarized in Table 1.

Table 1. Strategies for platelet count optimization to enable safe anticoagulation.

Stage	Management
Severe thrombocytopenia	Discontinue anticoagulation and control active bleeding, if present.
Treatment of thrombocytopenia	Initiate corticosteroids ± IVIG; if refractory, consider CYC, AZA, MMF, RTX, or TPO-RAs.
Anticoagulation-free phase	Use HCQ; implement mechanical antithrombotic measures; aspirin only if bleeding is controlled and platelets >30,000/mm³.
Resumption of anticoagulation	Once platelets >50,000/mm³ and bleeding resolved, restart anticoagulation (preferably LMWH, with subsequent transition to VKA).

**CYC — cyclophosphamide; AZA — azathioprine; MMF — mycophenolate mofetil; RTX — rituximab; TPO-RAs — thrombopoietin receptor agonists; LMWH — low-molecular-weight heparin; VKA — vitamin K antagonist.*

In catastrophic situations, when thromboembolic events involve at least three organ systems, initiation of combined therapy is mandatory and constitutes the first-line approach for CAPS [15,16]. This regimen encompasses full anticoagulation with heparin (whenever feasible), pulse corticosteroid therapy (methylprednisolone 500–1000 mg/day for three days), and plasmapheresis and/or IVIG [15,16]. Plasmapheresis reduces antibody burden and inflammatory mediators, while IVIG at a total dose of 2 g/kg (divided over 2–5 days) is indicated when plasmapheresis is not available [17]. In cases of refractory thrombocytopenia, IVIG carries the additional advantage of modulating the immune response and simultaneously elevating platelet counts. These components are detailed in Table 2.

Table 2. Combined therapy in Catastrophic Antiphospholipid Syndrome (CAPS).

Therapy Component	Description	Key Considerations
Full anticoagulation	Heparin (whenever possible)	Cornerstone of CAPS treatment; resume as soon as safely feasible.
Pulse corticosteroid therapy	Methylprednisolone 500–1000 mg/day for 3 days	Reduces intense inflammation and modulates the immune response.
Plasmapheresis	Removal of antibodies and inflammatory mediators	Indicated for rapid reduction of pathological immunological activity.
IVIG	Total dose of 2 g/kg divided over 2–5 days; used when plasmapheresis is not feasible.	Particularly useful in refractory thrombocytopenia; simultaneously raises platelet count and reduces autoimmune activity.

**CAPS — catastrophic antiphospholipid syndrome; IVIG — intravenous human immunoglobulin.*

Splenic embolization (SE) is primarily indicated in patients with ITP refractory to multiple pharmacological therapies, particularly when the patient is at high surgical risk or when dangerously low platelet counts render splenectomy hazardous. SE may also serve as a 'bridge' to splenectomy in patients with severe thrombocytopenia, transiently raising platelet counts to allow a safer subsequent procedure. Most authors recommend a preoperative platelet count above 50,000/mm³ to minimize hemorrhagic risk. A recent case report described a patient with refractory ITP and a platelet count of 4,000/mm³ with severe bleeding who underwent SE successfully, with platelet elevation observed the following day [18]. Although no universal consensus exists for SE, the procedure may be considered even in severe thrombocytopenia, particularly in emergency settings or when splenectomy is contraindicated.

The present case carries inherent limitations as a single case report; consequently, the clinical course and therapeutic outcomes reported herein cannot be generalized. Nonetheless, it highlights a scenario of extreme therapeutic complexity rarely encountered in clinical practice, in which the severity of the autoimmune process and its resistance to immune modulation — compounded by recurrent infectious complications from prolonged immunosuppression — rendered the condition persistently refractory, even in the face of aggressive and sequentially escalating interventions.

4. CONCLUSION

The association between CAPS and refractory ITP constitutes one of the most challenging clinical scenarios in autoimmune medicine, particularly due to the difficulty of reconciling elevated thrombotic risk with severe thrombocytopenia that precludes full anticoagulation. Adjunct antithrombotic strategies are indispensable during the period when anticoagulation cannot be safely employed. CAPS treatment is based on a combination of anticoagulation (whenever feasible), pulse corticosteroid therapy, and complementary therapies (plasmapheresis/IVIG).

Multiple efficacious and safe approaches exist for ITP management. Initial therapy is based on corticosteroids, alone or in combination with IVIG. In cases of inadequate response, immunosuppressants and targeted therapies (such as rituximab) alongside TPO-RAs may be incorporated. When refractoriness persists, procedural interventions such as splenectomy or splenic embolization may be considered. However, even under combined and intensive therapeutic strategies, a subset of patients may experience unfavorable outcomes, reflecting the complexity and severity of the underlying autoimmune process.

The trajectory of this case illustrates more than the severity of two coexisting autoimmune diseases: it reveals that despite multidisciplinary collaboration and the aggressive, timely, and coordinated application of multiple therapeutic strategies, clinical response may remain limited, exposing the boundaries of current clinical practice. Experiences such as this broaden our understanding of these conditions and reinforce the imperative for advances in the management of CAPS associated with refractory ITP, stimulating the development of novel therapeutic strategies.

REFERENCES

[1] ALMIZRAQ, R. J. et al. Efficacy and mechanism of intravenous immunoglobulin (IVIg) therapy in immune thrombocytopenia: a review. *Annals of Blood*, Hong Kong, v. 6, 2021. Disponível em: https://cdn.amegroups.cn/journals/vats/files/journals/29/articles/6137/public/6137-PB5-2485-R3.pdf. Acesso em: 7 dez. 2025.

[2] ATA, F. et al. Efficacy and safety of rituximab as second-line therapy in immune thrombocytopenia: a review. *British Journal of Haematology*, Oxford, v. 199, n. 2, p. 157–167, 2022. Disponível em: https://pmc.ncbi.nlm.nih.gov/articles/PMC9272691/. Acesso em: 7 dez. 2025.

[3] BITSADZE, V. et al. Catastrophic antiphospholipid syndrome: a comprehensive review. *Journal of Clinical Medicine*, Basel, v. 13, n. 3, 2024.

[4] EGABARIA, A.; BISHARAT, N. Splenic embolization in refractory immune thrombocytopenia. *European Journal of Haematology*, Copenhagen, v. 114, n. 5, p. 908–910, 2025. DOI: https://doi.org/10.1111/ejh.14391.

[5] ESPINOSA, G.; CERVERA, R. Catastrophic antiphospholipid syndrome: an update. *Hematology: American Society of Hematology Education Program*, Washington, DC, v. 2024, n. 1, 2024.

[6] GAFTER-GVILI, A. et al. Current approaches for the diagnosis and management of immune thrombocytopenia. *European Journal of Internal Medicine*, Amsterdam, v. 109, p. 7–15, 2023. Disponível em: https://www.ejinme.com/article/S0953-6205(22)00412-5/fulltext. Acesso em: 7 dez. 2025.

[7] GARRA, W. et al. Catastrophic antiphospholipid syndrome in lupus-associated immune thrombocytopenia treated with eltrombopag: case series and literature review. *Medicine (Baltimore)*, Baltimore, v. 102, n. 12, 2023.

[8] GRIMALDI, L. et al. Hydroxychloroquine and cardiovascular events in patients with systemic lupus erythematosus: a cohort study. *BMJ Open*, London, v. 14, 2024. Disponível em: https://pmc.ncbi.nlm.nih.gov/articles/PMC11364994/. Acesso em: 7 dez. 2025.

[9] NEUNERT, C. et al. American Society of Hematology 2019 guidelines for immune thrombocytopenia. *Blood Advances*, Washington, DC, v. 3, n. 23, p. 3829–3866, 2019. DOI: https://doi.org/10.1182/bloodadvances.2019000966.

[10] OKUNLOLA, A. O. et al. Catastrophic antiphospholipid syndrome: a review of current evidence and future management practices. *Cureus*, Palo Alto, v. 16, 2024. Disponível em: https://pmc.ncbi.nlm.nih.gov/articles/PMC11490264/. Acesso em: 7 dez. 2025.

[11] RODRÍGUEZ-PINTÓ, I. et al. Catastrophic antiphospholipid syndrome: the current management approach. *Journal of Autoimmunity*, London, v. 74, p. 1–7, 2016.

[12] RODRÍGUEZ-PINTÓ, I. et al. Plasma exchange in catastrophic antiphospholipid syndrome. *Therapeutic Apheresis and Dialysis*, Oxford, v. 23, n. 2, p. 105–109, 2019.

[13] SALTER, B. M.; CROWTHER, M. A. Catastrophic antiphospholipid syndrome: a CAPS-tivating hematologic disease. *Hematology: American Society of Hematology Education Program*, Washington, DC, v. 2024, n. 1, p. 214–221, 2024. DOI: https://doi.org/10.1182/hematology.2024000544.

[14] SHEN, N. et al. Thrombopoietin receptor agonists use and risk of thrombotic events in patients with immune thrombocytopenic purpura: a systematic review and meta-analysis of randomized controlled trials. *Biomedical Reports*, Athens, v. 20, n. 3, p. 44, 2024. DOI: https://doi.org/10.3892/br.2024.1732.

[15] SINISCALCHI, C. et al. Catastrophic antiphospholipid syndrome: a review. *Medicina*, Basel, v. 59, n. 1, 2023. Disponível em: https://www.mdpi.com/2673-5601/4/1/1. Acesso em: 7 dez. 2025.

[16] TEKTONIDOU, M. G. et al. EULAR recommendations for the management of antiphospholipid syndrome in adults. *Annals of the Rheumatic Diseases*, London, v. 78, n. 10, p. 1296–1304, 2019. DOI: https://doi.org/10.1136/annrheumdis-2019-215213.

[17] TJEPKEMA, M. et al. Risk of thrombosis with thrombopoietin receptor agonists for immune thrombocytopenia: systematic review and meta-analysis. *Critical Reviews in Oncology/Hematology*, Amsterdam, v. 174, 2022.

[18] VAN DE VONDEL, S. et al. Catastrophic antiphospholipid syndrome in an immune thrombocytopenia patient treated with avatrombopag: case report. *BMJ Case Reports*, London, v. 16, 2023.