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CASE REPORT

A Rare Case of Refractory Catastrophic Antiphospholipid Syndrome Successfully Treated With Rituximab and Plasma Exchange

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Abstract

A small subset of patients with antiphospholipid syndrome (APS) may develop widespread thrombotic disease with organ damage, referred to as catastrophic APS (CAPS) that is associated with a high mortality. Medical therapy typically involves a combination of anticoagulation, systemic glucocorticoids, plasmapheresis, and intravenous immune globulin (IVIG). There is currently no consensus for the management of refractory cases of CAPS. However, monoclonal antibodies such as rituximab and eculizumab have shown some benefits. Herein, we present a 29-year-old female with previous pulmonary embolism who presented with necrotic left toes and was eventually diagnosed with refractory CAPS, successfully treated with Plasmapheresis and Rituximab. With this case report, we hope to encourage the usage of Rituximab in the management of CAPS.

1. Introduction

Catastrophic antiphospholipid syndrome (CAPS) is an entity of antiphospholipid syndrome (APS) characterized by thromboses typically involving multiple small blood vessels in various organs rather than a large vessel deep vein thrombosis or stroke, although the latter can occur.[1] CAPS is frequently fatal, with a reported mortality rate approaching 50 percent despite anticoagulant and immunosuppressive treatment.[2] Thus, early diagnosis and aggressive therapy is essential to the management of CAPS. Nevertheless, there are currently no consensus in the treatment of patients with CAPS refractory to conventional medical therapy.[3] We report the case of a 29-year-old female who presented with left toes ischemia and was later found to have CAPS, successfully treated with the addition of Rituximab to the conventional medical therapy. We hope to encourage and consolidate the use of Rituximab in the management of refractory CAPS.

2. Case presentation

This a 29-year-old female with past medical history of poorly controlled Diabetes Melitus, Deep Vein Thrombosis (DVT) and Pulmonary Embolism (PE) who presented for evaluation of a 7-day history of painful bluish discoloration of the first 3 digits of the left foot. Of note, 2 years prior to our encounter, the patient was admitted for hypoxic respiratory failure due to COVID-19 infection. Admission during which, she developed DVT and PE. She was then discharged on Rivaroxaban for 3 months as the PE was thought to be provoked by the COVID-19 infection. The patient denied any previous miscarriages.

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Upon arrival in the Emergency Department, she was found to be hemodynamically stable but in excruciating pain. Physical examination was marked by cyanosis of the first 3 toes of the left foot. She was found to have elevated Partial Thromboplastin Time (PTT) and Prothrombin Time (PT) that did not correct with mixing study as seen in Table 1. Arterial Doppler of the lower extremity revealed occlusion of the left proximal superficial femoral artery to proximal Popliteal arteries, with reconstitution at the distal popliteal artery and the Tibial Peroneal trunk could not be visualized. She was started on heparin continuous infusion and vascular surgery was consulted. She underwent a subsequent left lower extremity angiogram that confirmed the occlusions.

She then underwent a Femoral thromboendarterectomy and a left femoral artery to posterior tibial artery bypass with autologous left great saphenous vein. 2 days following the surgery, the patient was found to have absent pedal pulses of the left lower extremity (LLE), she was taken for emergent angiogram during which she underwent a mechanical thrombectomy of the bypass of the left anterior tibial artery and left posterior artery.

The day following the angiogram, LLE pulses were again found to be diminished. Hematology was consulted and work up for antiphospholipid syndrome (APS) was ordered. Heparin continuous infusion was titrated with anti-Factor Xa nomogram. The patient was eventually found to have a positive workup for APS as seen in Table 1. Given the recurring nature of the arterial thromboses, the patient was started on Methylprednisolone.

The patient's LLE pain continued to worsen despite 2 previous vascular interventions, thus a revision was planned. She then underwent an LLE interposition popliteal to Anterior Tibial bypass using contralateral Saphenous Vein Grafts (SVG) and thrombectomies of newly found clots. The patent was switched to argatroban given new clots developed while on heparin. The patient was started on plasmapheresis (PLEX) for 5 days and intravenous immune globulin (IVIG) per hematology recommendation.

On day of 16 hospitalization, following treatment with PLEX, IVIG and while on argatroban, the patient was found to be tachycardic and hypoxic; a Computed Tomography (CT) of the Chest revealed a Pulmonary Embolism. PLEX was restarted for 5 additional doses, weekly Rituximab was added to the regimen, and Argatroban was switched to low molecular weight Heparin (LMWH). The patient eventually underwent a Left Trans metatarsal Amputation with Achilles tendon lengthening. The patient's respiratory failure gradually improved, and her coagulation studies had normalized. She showed continued clinical improvement and was discharged to a rehabilitation facility after 34 days of hospitalization.

3. Discussion

Catastrophic antiphospholipid syndrome (CAPS) is a severe and frequently fatal manifestation of antiphospholipid syndrome (APS) that affect only 1% of patients with APS.[4] Thromboses are the hallmark of APS, and venous thromboses are more common than arterial thromboses.[5] Our patient had a previous Deep Vein Thrombosis (DVT) and Pulmonary Embolism (PE), she should have been evaluated for hypercoagulability. However, the PE was felt to be provoked by COVID-19 induced coagulopathy and was only on anticoagulants for secondary prevention. Cessation of prior anticoagulation has been recognized as a precipitating factor of CAPS.[6] This was the case in our patient.

Table 1. Summary of diagnostic work-up during hospitalization.

	Lab values	Lab values upon mixing
Partial Thromboplastin Time (PTT)	**100.06 s (25.1–34.4)**	**62.8 s (23.4–38.9)**
Prothrombin Time (PT)	**18.3 s (12.5–14.4)**	**14.50 s (12.20–14.40)**
B2 Glycoprotein I (IGG) antibody (AB)	**>112.0 units per milliliter (U/mL) (<20.0)**	
B2 Glycoprotein I (IGM) AB	9.7 U/mL (<20.0)	
B2 Glycoprotein I (IGA) AB	**40.6 U/mL (<20.0)**	
Cardiolipin AB (IGA)	**48.7 APL-U/mL (<20.0)**	
Cardiolipin AB (IGG)	**>112.0 APL-U/mL (<20.0)**	
Cardiolipin AB (IGM)	9.6 MPL-U/mL (<20.0)	
Lupus anticoagulant profile	**Positive for lupus anticoagulant**	
Blood Urea Nitrogen	10 mg per deciliter (mg/dL) (7–25)	
Creatinine	0.6 (0.6–1.20)	
Aspartate aminotransferase	23 Unit per liter (U/L) (13–39)	
Alanine transaminase	31 U/L (7–52)	
Total bilirubin	0.4 mg/dL (0.3–1.0)	

Diagnostic criteria for CAPS include evidence of involvement of at least three organs, systems, or tissues; development of manifestations simultaneously or in less than 1 week; histopathologic confirmation of small-vessel occlusion; and laboratory confirmation of the presence of Antiphospholipid (aPL) antibodies. A Lupus Anticoagulant (LA) is present in 81.7% of patients, and the anticardiolipin antibodies Immunoglobulin G (aCL IgG) is the most common positive aPL antibody.[6] Our patient developed multiple arterial and venous thromboses, simultaneously and within a week of each other's. She was also found a LA and the aCL IgG was quite elevated during her hospitalization.

Aggressive treatment in CAPS has reduced mortality rate from approximately 50% to approximately 20%.[7] A triple-therapy strategy of anticoagulation, glucocorticoids, and either intravenous immune globulin (IVIG) or plasma exchange is currently recommended.[8] For patients with refractory CAPS, either rituximab (B-cell depletion) or eculizumab (complement inhibition) treatment have been considered.[9] Our patient was started on the triple-therapy strategy once the presumptive diagnosis of CAPS was made. However, she relapsed developing a PE while on the triple therapy. Addition of Rituximab prevented any further relapse. We propose early use of Rituximab in the management of CAPS as this condition is associated with high mortality without proper management.

4. Conclusion

Catastrophic antiphospholipid syndrome (CAPS) is a rare but fatal manifestation of antiphospholipid syndrome (APS). Early aggressive management has shown to reduce mortality. Rituximab has been used in refractory cases and has shown benefits as this was the case with our patient. With this case report, we hope to encourage early use rather than delayed use of Rituximab in conjunction with Plasma exchange int the management of CAPS.

Ethics approval

This study protocol was reviewed and the need for approval was waived by the ethics committee at Palisades Medical Center Hackensack Meridian Health.

Consent for publication

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

Availability of data and materials

All data generated or analyzed during this study are available from the corresponding author upon request.

Conflict of interest

Not applicable.

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Authors' contributions

Ayrton Bangolo searched the literature, wrote, and revised the manuscript. Sowmya Sagireddy, Sarah Mahamadeen, Felicia Hasta, Sadhu A. Reddy, Afshan Naz, Ravishankar Ranganatha, Cleveland Ricketts, Padmavathi Muppalla, Swathi Veliginti, Georgemar Arana, Dily T. Sathyarajan, Sachin Singh, Tanvi Shetty, Kshitij Bhardwaj, Sayed Hashemy, Roberto L. Duran, Sung H. Kim, Candice M. Hipolito, Kibo Yoon, Vrusha Patel, Aseel Alshimari, Pugazhendi Inban, Saaniya Yasmeen revised and edited the manuscript. Simcha Weissman approved the final version and is the article's guarantors. All authors certify that they contributed sufficiently to the intellectual content and data analysis. Each author has reviewed the final version of the manuscript and approves it for publication.

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