Case Report

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Report of plasma exchange in a rare case of association of myasthenia gravis with thymoma and parathyroid adenoma

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Abstract:

Myasthenia with thymoma and parathyroid adenoma is a rare presentation. Very few cases have been reported of this association without much role of plasma exchange in these patients. Here, we present our experience of plasma exchange in this rare clinical entity.

Keywords:

Myasthenia gravis, parathyroid adenoma, plasma exchange, thymoma

Introduction

Plasma exchange (PE) is established modality for myasthenia gravis crisis and myasthenia exacerbation (Category I) as per American Society for Apheresis (ASFA).[1] Rarely, myasthenia with thymoma can be associated with parathyroid adenoma, and only few such cases had been reported in the literature[2-5] with none describing the experience of PE in these patients as hypercalcemia due to hyperparathyroidism poses a big challenge to maintain anticoagulation in extracorporeal circuit due to deranged calcium hemostasis. Here, we present our experience of therapeutic PE in this rare clinical entity including the problems faced during procedures.

Case Report

A 33-year-old male known case of myasthenia gravis was admitted at our hospital with presenting complaints of diplopia and shortness of breath for 1 month and weakness of both limbs for 3 days. He had a history of similar episode 3 years back (2018) for which prednisolone 40 mg for 15 days was given at a local hospital. One year later, he got admitted at our hospital with complaints of low-grade fever associated with chills and rigor and bilateral upper and lower limb weakness. The patient was diagnosed with myasthenia gravis with Acetylcholine receptor antibody positive (AChR Ab+ ≥80) and started on mycophenolate mofetil 500 mg BD, prednisolone 40 mg, and pyridostigmine 60 mg three times a day. Contrast-enhanced computed tomography chest showed thymoma (3.8 cm × 2.2 cm). The patient was referred to the department of transfusion medicine for PE. Three procedures of PE were done on alternate days before thymectomy.

In January 2021, the patient again presented with sign and symptoms of myasthenia crisis. He had dyspneic episodes which worsened at rest with altered sensorium and severe weakness of limbs unable to roll over bed. No response to steroids and

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intravenous (IV) immunoglobulin was seen and crisis precipitated. Hence, decision for PE was taken.

Baseline laboratory profile including complete blood counts (hemoglobin = 120 g/L, total leukocyte count = 11 × 10^9/L, and platelet = 307 × 10^9/L), renal function test (blood urea = 18.64 mmol/L and serum creatinine = 79.56 µmol/L) liver function test (aspartate transaminase/alanine transaminase/alkaline phosphatase = 0.35/1.60/0.97 µkat/L), coagulation profile (prothrombin time [PT]/activated partial thromboplastin time [APTT]=13.6 s/24 s), and preprocedure ionized calcium (ical = 1.13 mmol/L) were within the normal range. Three PE procedures were attempted through central line but could not be completed due to clot formation in extracorporeal circuit during the procedure [Table 1]. In the first procedure, we observed multiple alarms due to low inlet and high return pressure and procedure paused multiple times. Central line as well as inlet/return lines was flushed frequently with saline and heparin, but due to multiple clots in the circuit, procedure could not be continued and was terminated. For the next procedure, new central line insertion was advised to clinician. The second procedure was initiated with fresh lot of disposables, initial inlet flow was satisfactory but after 723 ml of plasma exchanged, return pressure high alarms started appearing. Both inlet and return lines were flushed multiple times, but multiple clots formation was observed in the entire circuit [Figures 1a and b], so procedure was aborted. Coagulation profile was normal with PT, APTT, PTI as 12 s, 32 s, and 85%, respectively. Keeping in mind the deteriorating condition of patient and nonresponsiveness to medical therapy, third procedure was planned using combination of heparin and Anticoagulant citrate dextrose solution (ACD-A). 5U/ml of heparin was added in 500 ml of ACD and Inlet Anticoagulant (AC) ratio was kept as 24:1. Kit with new lot number was taken, initially procedure started smoothly but at 709 ml of plasma exchanged, clot formation started, so, additional 2U/ml of heparin was added to ACD-A and WB: AC ratio was increased to 20:1. Multiple attempts were made by flushing the central line and lines of circuit but procedure was terminated due to multiple alarms and no flow in circuit due to clots.

The patient was advised for Sonoclot, serum calcium levels, and parathyroid hormone (PTH) levels.

Further follow-up and management

Sonoclot revealed hypercoagulability pattern with decreased R time and increased maximum amplitude. There was persistent rise in serum calcium with each day. PTH level was 248 pg/ml (15–65 pg/ml), 24-hour urinary calcium was also raised to 373 mg/day (50-300 mg/day). Tc-99 m Sestamibi scintigraphy was done which revealed left inferior parathyroid adenoma. PET scan was normal. The patient was diagnosed with "Myasthenia gravis with Hypercoagulability due to parathyroid adenoma". Rituximab 1 g IV was given twice to patient in gap of 15 days in view of persistent ventilatory support. He was managed with hydration, Vitamin D supplementation, and calcitonin. The patient was discharged after 40 days on oral pyridostigmine, steroids, and multivitamins with normal serum calcium levels (9.25 mg/dl).

Discussion

This case illustrates the challenges observed during PE in a rare combination of myasthenia gravis with parathyroid adenoma with hypercalcemia. Calcium acts as a cofactor in extrinsic and common coagulation pathways by conversion of prothrombin to thrombin, activation of coagulation factor V and VIII.[6] Standard anticoagulation solutions contain citrate which efficiently prevents blood clotting by chelation of calcium and other metal ions which leads to conformational changes of the coagulation factors V and VIII resulting in loss of its procoagulant activity.[7] In the extracorporeal circuit, citrate concentrations of 15-24 mmol/L reduce ionized Ca^{2+} levels sufficiently (to 0.2 – 0.3 mmol/L) to impair hemostasis and produce an anticoagulant effect.[7] In this case, there was an unregulated overproduction of PTH which resulted in irregular homeostasis of calcium resulting in clot formation in extracorporeal circuits during all the

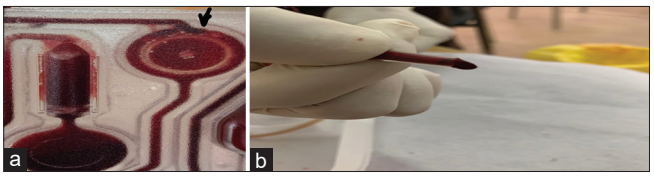

Figure 1: (a) Image of disposable kit showing microclot (arrow) (b) cut section of tubing of disposable kit showing clot

Table 1: Details of therapeutic plasma exchange procedures

Procedure number	Plasma volume exchanged (ml)	Reason for termination	Anticoagulant used	Inlet AC ratio
1	209	Entire circuit clotted	ACD-A	10:1
2	723	Multiple clot formation in extracorporeal circuit	ACD-A	12:1-10:1
3	709	Entire circuit clotted	ACD-A and heparin	24:1

ACD-A=Anticoagulant citrate dextrose solution

three PE procedures. Moreover, we tried combination of ACD-A and heparin in the third procedure as has been previously described by DeSimone *et al*.[8] but was not of much use in our case. A study done by Koufakis *et al*. has also demonstrated thrombotic event in three patients with primary hyperparathyroidism due to parathyroid adenoma similar to our observation of clotting in extracorporeal circuit of PE kit in this patient during PE.[9]

Conclusion

A complete laboratory profile including a total baseline calcium level assessment must be performed in all the patients requiring therapeutic PE, especially in the event of an extracorporeal clot formation during the procedure. Appropriate and adequate anticoagulation of the patient with the agents having different anticoagulant mechanism may help in patients as frequent and premature termination of PE procedure can become cumbersome for the patient and may add overall financial burden in the management of such case.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

References

1. Padmanabhan A, Connelly-Smith L, Aqui N, Balogun RA, Klingel R, Meyer E, *et al.* Guidelines on the use of therapeutic apheresis in clinical practice-Evidence-based approach from the Writing Committee of the American Society for Apheresis: The eighth special issue. J Clin Apher 2019;34:171-354.
2. Triggiani V, Guastamacchia E, Lolli I, Troccoli G, Resta F, Sabbà C, *et al.* Association of a wide invasive malignant thymoma with myastenia gravis and primary hyperparathyroidism due to parathyroid adenoma: Case report and review of the literature. Immunopharmacol Immunotoxicol 2006;28:377-85.
3. Dubner S, Zhukhovitskaya A, Zeltsman D. Parathyroid Adenoma/Thymoma case report. Clin Surg 2017;2:1525.
4. Maria V, Saad AM, Ioannis F. Parathyroid adenoma associated with thymoma in a female adult with primary hyperparathyroidism. Int J Surg Case Rep 2013;4:105-7.
5. Palin SL, Singh BM. Primary hyperthyroidism due to a parathyroid adenoma with subsequent myasthenia gravis. QJM 2000;93:560-1.
6. Quick AJ, Stefanini M. The chemical state of the calcium reacting in the coagulation of blood. J Gen Physiol 1948;32:191-202.
7. Strauss RG. Mechanisms of adverse effects during hemapheresis. J Clin Apher 1996;11:160-4.
8. DeSimone RA, Myers GD, Guest EM, Shi PA. Combined heparin/acid citrate dextrose solution A anticoagulation in the Optia continuous mononuclear cell protocol for pediatric lymphocyte apheresis. J Clin Apher 2019;34:487-9.
9. Koufakis T, Antonopoulou V, Grammatiki M, Karras SN, Ajjan R, Zebekakis P, *et al.* The relationship between primary hyperparathyroidism and thrombotic events: Report of three cases and a review of potential mechanisms. Int J Hematol Oncol Stem Cell Res 2018;12:175-80.