Successful therapeutic plasma exchange in a patient with Morvan syndrome

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Abstract:
Morvan syndrome is a rare autoimmune disorder, characterized by hyperexcitability of both central and peripheral nervous systems, accompanied by autonomic dysfunction and hallucinations. Therapeutic plasma exchange (TPE) has been found to be an effective mode of treatment for this disease, but there is limited literature supporting the same. A 26-year-old male was admitted to our hospital and diagnosed with a case of Morvan syndrome, based on the clinical picture and laboratory findings. When standard drug therapy failed to show any improvement, a decision to carry out TPE was taken. The case presented with many peculiar challenges, mostly due to autonomic instability and hyperkinesia experienced by the patient while carrying out the procedure. All these challenges were diligently addressed and managed promptly. Clinical signs of improvement were evident from the 2nd TPE and by the time fifth TPE had finished, the patient was able to perform activities such as walking with support. His autonomic dysfunction and behavioral abnormalities had significantly subsided. This case report highlights the possible effectiveness of TPE in the management of a rare disease such as Morvan syndrome and appropriate application of basic principles and criteria for the use of TPE in cases where limited literature is available.

Keywords:
Complications of therapeutic plasma exchange, successful outcome of therapeutic plasma exchange, therapeutic apheresis, therapeutic plasma exchange in rare neurological disorders

Introduction
Morvan syndrome is a debilitating neurological disorder, characterized by irregular jerky movements, weakness of muscles, excessive sweating, tachycardia, and hypertension. Presence of neuropsychiatric features such as hallucinations differentiates it from other diseases which fall under the broad category called neuromyotonias. Neuromyotonia can be described as generalized peripheral nerve hyperexcitability, which may clinically result in fasciculation, muscle cramps, pain, and stiffness. The underlying cause has been identified to be raised serum autoantibodies against voltage-gated potassium channels (VGKCs) and anti-contactin-associated protein 2 (CASPR2) antibody, a subtype of VGKC considered be the hallmark of Morvan syndrome. It was first described in 1890 by the French physician A.M. Morvan.

Case Report
A 26-year-old male was admitted at our center with a short history of febrile illness of 1-week duration. He had gradually progressive symptoms of involuntary, hyperkinetic movements and weakness of both upper and lower limbs. Autonomic dysfunction had manifested in the form of excessive sweating and insomnia. Behavioral...
abnormalities along with auditory hallucinations were also present.

General examination findings revealed signs of autonomic dysfunction as his resting pulse rate remained consistently above 110 beats/min, whereas his blood pressure was found to be frequently elevated above 160/100 mm of Hg. Wasting of muscles of all four limbs was also evident.

Laboratory investigations initially unveiled hypokalemia (serum potassium: 3.2 mEq), with hypoproteinemia (total protein: 5.8 g/dl, albumin: 3.8 g/dl, and globulin: 2.0 g/dl).

He was further evaluated for possible causes of neuromyotonia. The patient had a positive serum anti-CASPR2 antibody, a subtype of VGKC complex detected by using immunofluorescence method and considered to be the hallmark of Morvan syndrome.\(^6\)

Initial treatment with high-dose steroids and intravenous immune globulin (IVIG) for 2 weeks offered no improvement in his condition. Given progression of the disease, decision to carry out therapeutic plasma exchange (TPE) was considered. As per the latest ASFA guidelines (2016), <100 cases have been reported in the literature,\(^7\) where TPE has been used as a treatment option for reducing antibodies against VGKC. Morvan syndrome also falls under this broad category of neurological disorders and a Category II indication for carrying out TPE. A thorough review of literature was carried out and considered in context of McLeod’s criteria, which states if the disorder’s pathophysiology is understood and the apheresis procedure could modify it, the risk–benefit ratio of carrying out TPE should be evaluated. The same was done for this patient and as the potential benefits outweighed the risks, the decision to carry out the procedure was considered appropriate.\(^8\)

A double-lumen femoral line was placed under strict aseptic precautions for carrying out TPE, using MCS plus 9000 (Hemonetics, Unites States) apheresis platform. Another peripheral venous access was established for infusion of calcium. Patient’s potassium levels were corrected before the start of the procedure. FFP and saline were chosen as the replacement fluid (in the ratio of 70:30). Although albumin is considered the ideal replacement fluid, it could not be used in this case due to financial constraints of the patient. The procedure was carried out in an Intensive Care Unit in view of abnormal vital parameters. Patient’s total plasma volume was calculated as per his body weight, and 100% of this total plasma volume was exchanged (1 plasma exchange) on alternate days for five sessions of TPE.

The process of carrying out TPE proved to be very challenging from the 1st cycle. Persistent hyperkinetic movements of all the limbs caused recurrent hindrance to the flow through femoral line and tubing. The process had to be paused intermittently to manually rectify the obstruction and restore normal flow. Constant vigil on tubing was required to avoid kinks and maintain a normal flow rate. Later, the patient had to be restrained by cuffing the limbs, after obtaining consent from his relatives. Tablet methyl prednisolone was also given to the patient as part of the management along with tablet clonazepam for its antiepileptic as well as sedative effect.

The patient developed an allergic reaction to FFP during the first sitting itself in the form of rashes over entire body which subsided on treatment with antihistamines. Rest of the TPE sessions were carried out after premedicating the patient with antihistamines, and allergic reaction to FFP was not observed again.

Due to persistently elevated blood pressure (>160/100 mm of Hg) and tachycardia (>110 bpm), any further rise in his vital parameters during the procedure could have been detrimental. To ensure optimum safety of the patient, the entire procedure was carried out in an Intensive Care Unit, and an intensivist was on standby in case of any eventuality.

His serum protein was on lower side (5.2 g/dL) before the start of TPE. The patient was also transfused with four units of FFP postprocedure, after each TPE session. This enhanced FFP support rectified his total serum proteins (7.2 g/dL) before the fourth TPE commenced. Flow rate and amount of fluid exchanged were kept at lower levels during each exchange cycle, using apheresis bowl of a lower volume (125 ml) to ensure that the patient remained hemodynamically stable.

**Results and Discussion**

Clinical signs of improvement were evident after 2nd TPE, as he was able to sit with support. After fifth TPE, he was able to carry out activities such as eating and walking with support. Only mild, occasional hyperkinetic movements were observed. His autonomic dysfunction had significantly improved, and his pulse rate was below 90 beats/min and blood pressure had returned to levels below 140/90 mm of Hg. Excessive sweating, restlessness, and insomnia had completely subsided. There were no behavioral abnormalities observed in the patient. The titers of anti-CASPR2 antibodies had also declined from 1:128 (before the start of the procedure) to 1:16 after the final TPE session was over (normal level: <1:10). TPE proved to be instrumental in his management and provided optimum
results, while other treatment modalities offered little improvement.

Various treatment modalities such as the use of immunosuppressive drugs, IVIG, and TPE have proved to be successful in treating VGKC-associated limbic encephalitis.\[^9\] There is no single established treatment protocol, and the approach which benefits the patient most should be followed. TPE is usually more effective in lowering the circulating antibody titers in the acute phase of disease while immunosuppressive drugs form the mainstay of long-term management.\[^10\] In this case, TPE was considered as an option only when the patient had shown no improvement with high-dose steroids and IVIG during the initial phase of treatment. He was treated with oral prednisolone (1 mg/kg/day) for a period of 6 months following improvement in his symptoms and remained in remission.

**Conclusion**

In the absence of established guidelines and the availability of limited literature while managing a rare disease, the application of basic principles and criteria for the use of TPE as a treatment modality should always be considered.\[^8\] This case further reiterates the effectiveness of TPE in the management of a rare disease such as Morvan syndrome.

**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.

**Financial support and sponsorship**

Nil.

**Conflicts of interest**

There are no conflicts of interest.

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