SERONEGATIVE IMMUNE-MEDIATED NECROTIZING MYOPATHY WITH RHABDOMYOLYSIS-INDUCED ACUTE KIDNEY INJURY: THE ROLE OF MEDIUM CUT-OFF MEMBRANE DIALYSIS

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INTRODUCTION

- Immune-mediated necrotizing myopathy (IMNM) is a rare, severe form of inflammatory myopathy characterized by prominent muscle fiber necrosis, progressive proximal muscle weakness, and markedly elevated creatine kinase (CK) levels. Rhabdomyolysis is one of the most important complications of the disease.
- Extracorporeal removal of myoglobin was not routine treatment in rhabdomyolysis-induced AKI. However, our case highlights the effective treatment with the medium cut-off (MCO) membrane for myoglobin removal and complete renal recovery.

CASE PRESENTATION

- A 79-year-old woman with a history of hypertension and type 2 diabetes mellitus with diabetic kidney disease (DKD) presented with 5 days of acutely progressive painful bilateral proximal limb weakness and oliguria. Neurological findings showed drowsiness and proximal muscle weakness, graded as MRC scale 2. There were no rashes or joint inflammation.
- Initial laboratory results revealed a creatine kinase (CK) level of 30,169 IU/L, serum Cr 7.96 mg/dL, and BUN 124 mg/dL (Table 1). Myositis-specific antibodies, including anti-SRP and anti-HMG-CoA reductase, were negative. An electromyogram indicated diffuse and active irritable myopathy. Muscle biopsy showed multiple pale necrotic fibers with lymphocytic and macrophage infiltration, along with diffuse p62 positivity.
- The diagnosis was seronegative IMNM, with rhabdomyolysis-induced AKI.
- Acute intermittent hemodialysis (IHD) was initiated due to uremia and specific treatment with intravenous methylprednisolone (IVMP) and immunoglobulin (IVIG) for five consecutive days. After complete treatment with intravenous methylprednisolone for 5 days and the 3rd day of IVIG treatment, CK levels were still rising, and no renal recovery. We applied a medium cut-off dialyzer (Theranova®) for myoglobin removal in a total of 6 hemodialysis sessions.

RESULT

- Patient muscle weakness gradually improved, and CK levels dramatically reduced within two weeks (Table 1). Additionally, there was an increase in urine output, renal function was recovered, and hemodialysis was discontinued within three months of follow-up.

MUSCLE HISTOPATHOLOGICAL FINDING

- The muscle biopsy review shows myopathic changes with necrotizing myosin. Presence of multiple scattered pale necrotic/degenerated fibers with CD3 positive lymphocytic and macrophage infiltration with diffuse P62 positivity.

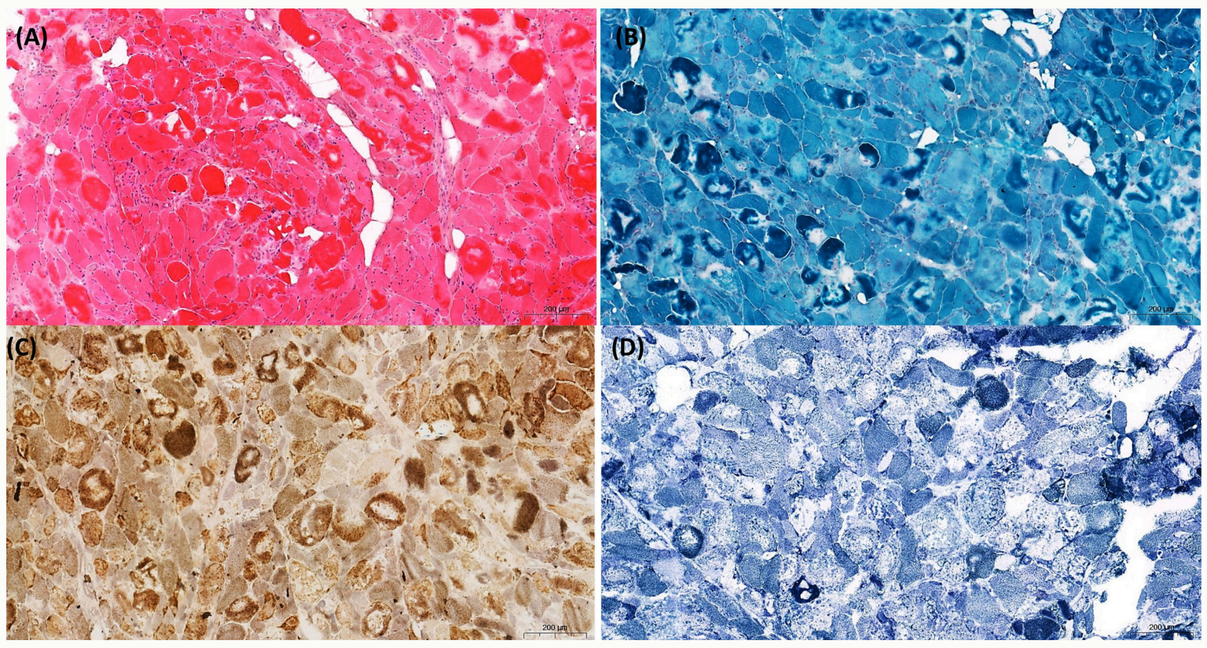

Fig.1 (A) H&E and (B) mGT : Demonstrate marked variation in fiber size, degenerated fibers, (C) COX/SDH : many COX-negative fibers, (D) NADH-TR: disturbed/damaged muscle fibers

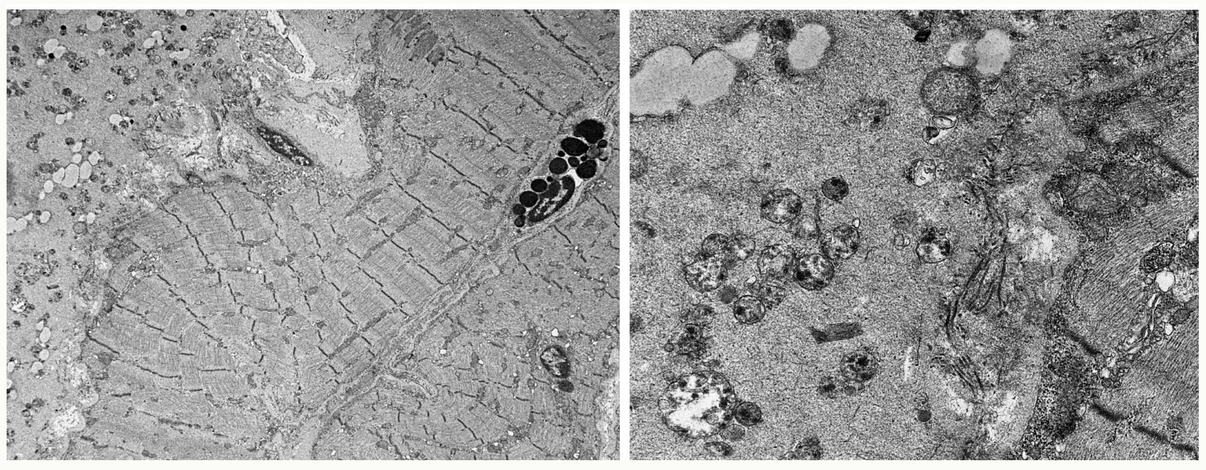

Fig.2 Electron microscopy reveals evidence of myonecrosis and destructive mitochondria

DISCUSSION

- Rhabdomyolysis is one of the most severe complications of IMNM.
- Myoglobin, a 17 kDa intrinsic protein found in muscle cells, is the primary mediator of rhabdomyolysis-induced acute kidney injury. Its pathogenic effects occur through renal vasoconstriction, intratubular cast formation, and direct tubular cell toxicity.
- Creatine kinase (CK), an intrinsic enzyme of skeletal muscle, does not directly correlate with myoglobin-induced nephrotoxicity or acute kidney injury; however, its circulating levels serve as a quantitative marker for the severity of rhabdomyolysis
- Theranova® is a single-use hollow-fiber dialyzer equipped with a medium cut-off (MCO) membrane, which enables more efficient clearance of larger middle molecules, including myoglobin, and can lead to recovery of renal function and discontinuation of dialysis, as demonstrated in this case.

Table 1. Clinical Characteristics and Laboratory Investigation

Date of admission	Day 1	Day3	Day 5	Day 9	Day 11	Day 16	After discharge 12 weeks
BP (mmHg)	120/65	110/60	137/58	131/64	148/73	147/65	106/61
Urine I/O (ml)	1050/75	1050/134	250/35	900/134	750/210	878/160	1000/1000
BUN (mg/dL)	124	134	92	92	74	73	31
Creatinine (mg/dL) Cr at baseline 1.78	7.96	9.41	7.08	3.98	2.71	3.27	1.24
CK level (IU/L)	30,169	27,014	24,940	32,062	41,202	912	16
Motor power at MRC grading	Proximal gr II Distal gr IV	Proximal gr II Distal gr IV	Proximal gr II Distal gr IV	Proximal gr II Distal gr IV	Proximal gr II Distal gr IV	Proximal gr II Distal gr IV	**Proximal gr IV Distal gr IV**
Management	Crystalloids resuscitation	Start IVMP 1 g for 5 days	Initiate hemodialysis	Complete IVMP for 5 days	Start IVIG 2 g/kg/5 days	Start oral prednisolone 30 mg/day	Continue mycophenolate 1 g/day and prednisolone 10 mg/day
Dialyzer type	ELISIO 15L	ELISIO 15L	ELISIO 15L	ELISIO 15L	Theranova ®	Theranova®	Theranova®

BP = Blood pressure, BUN = blood urea nitrogen, CK = Creatine kinase (CK), Urine I/O = urine input and output
IVMP = Intravenous methylprednisolone, IVIG = Intravenous Immunoglobulin

CONCLUSION

- This case report highlights the potential utility of medium cut-off (MCO) membrane hemodialysis as an adjunctive therapy, in conjunction with disease-specific treatments and conventional supportive care.

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