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Rescue Therapy in Refractory Shock: The Role of Methylene Blue in Septic Vasoplegia

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Introduction

Methylene blue has emerged as an effective rescue therapy in refractory septic shock, particularly when conventional vasopressor support fails to restore adequate perfusion. By inhibiting nitric oxide synthase and guanylate cyclase, it targets the nitric oxide–cGMP pathway, reversing vasodilation and stabilizing hemodynamics, which facilitates weaning from high-dose vasopressors. We present a case that illustrates its utility in managing persistent vasoplegia in severe septic shock.

Case Description

A 63-year-old man with diabetes, hypertension, dyslipidemia, and end-stage renal failure on regular hemodialysis presented with two days of generalized weakness, vomiting, and abdominal pain. Initially, his vitals were stable (GCS E4V5M6, BP 140/54 mmHg, HR 90 bpm); however, he quickly deteriorated (GCS E3V4M6) and developed non-fluid-responsive hypotension (BP 87/45 mmHg), necessitating inotropic support. A venous blood gas revealed severe high anion gap metabolic acidosis (pH 6.6, HCO_3^- 2.2 mmol/L, lactate 25 mmol/L). The patient was intubated, and emergency hemodialysis was initiated. Laboratory results showed leucocytosis (TWC 32 ×10⁹/L) and markedly elevated amylase (1322 U/L), while CT imaging of the abdomen revealed diffuse colonic wall thickening. Diagnosed with severe septic shock secondary to pancreatitis, he remained hypotensive despite triple hemodynamic support. Intravenous methylene blue was administered 21 hours after admission for refractory vasoplegia. The patient was managed in the ICU for six days, gradually weaned off hemodynamic support, underwent multiple CVVH sessions, and showed metabolic improvement. He was discharged in stable condition on day 15.

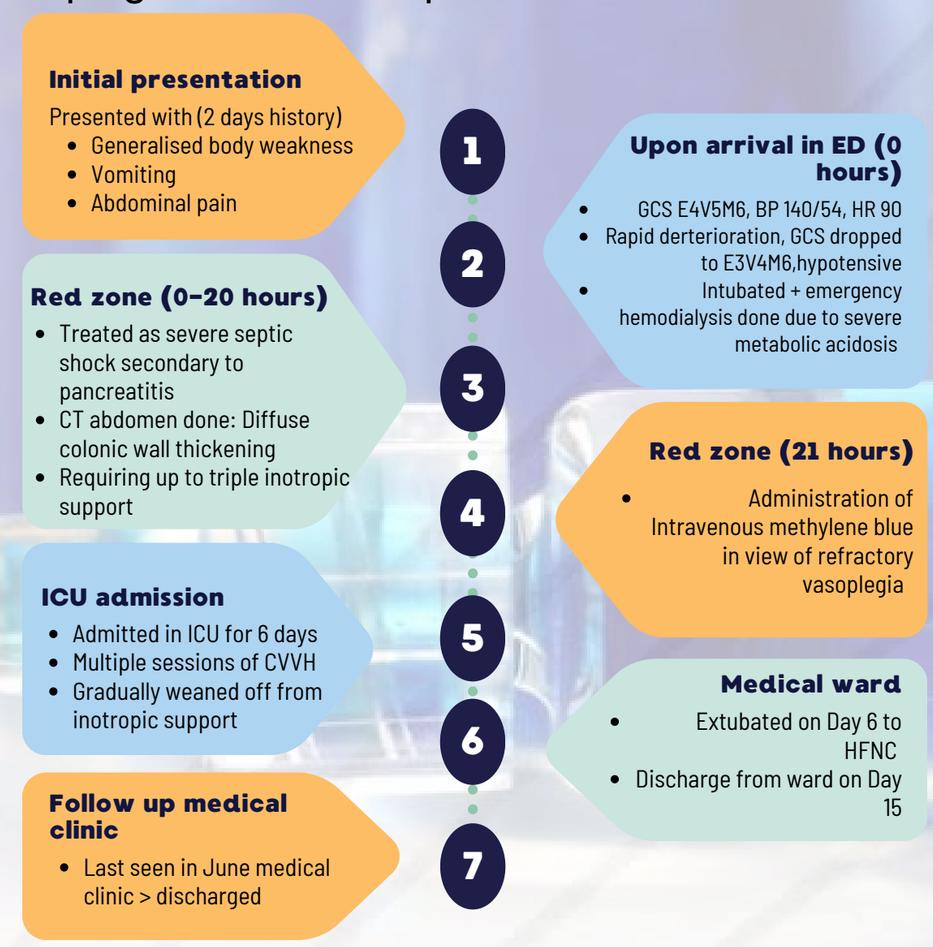

Figure 1: Timeline of events

ABG Trend	D1 (ED) Upon arrival (4 hrs)	D1 (ED) Post SLED (3 hrs)	D2 (ICU) Post methylene blue + CVVH
pH	6.6	6.8	7.3
HCO3	2.2	5.7	17.0
Lactate	25.0	17.0	2.69

Figure 2: Serial ABG trend

Discussion

This case highlights the complexity of managing refractory septic shock in the setting of severe lactic acidosis and vasoplegia. Profound acidosis likely impaired beta-adrenergic receptor responsiveness, diminishing the efficacy of conventional catecholamine vasopressors. Methylene blue (MB) served as an effective adjunct by inhibiting nitric oxide synthase and guanylate cyclase, thereby restoring vascular tone through the nitric oxide–cGMP pathway. Its administration resulted in improved mean arterial pressure and facilitated weaning from triple inotropic support, marking a key turning point in hemodynamic recovery. Although used off-label, MB has shown promise in treating vasoplegic syndromes, especially when adrenergic agents fail. Compared to non-selective nitric oxide inhibitors, MB offers targeted reversal of vasodilation while preserving some physiological NO effects. Its role remains adjunctive, not definitive, and should be supported by source control and standard critical care.

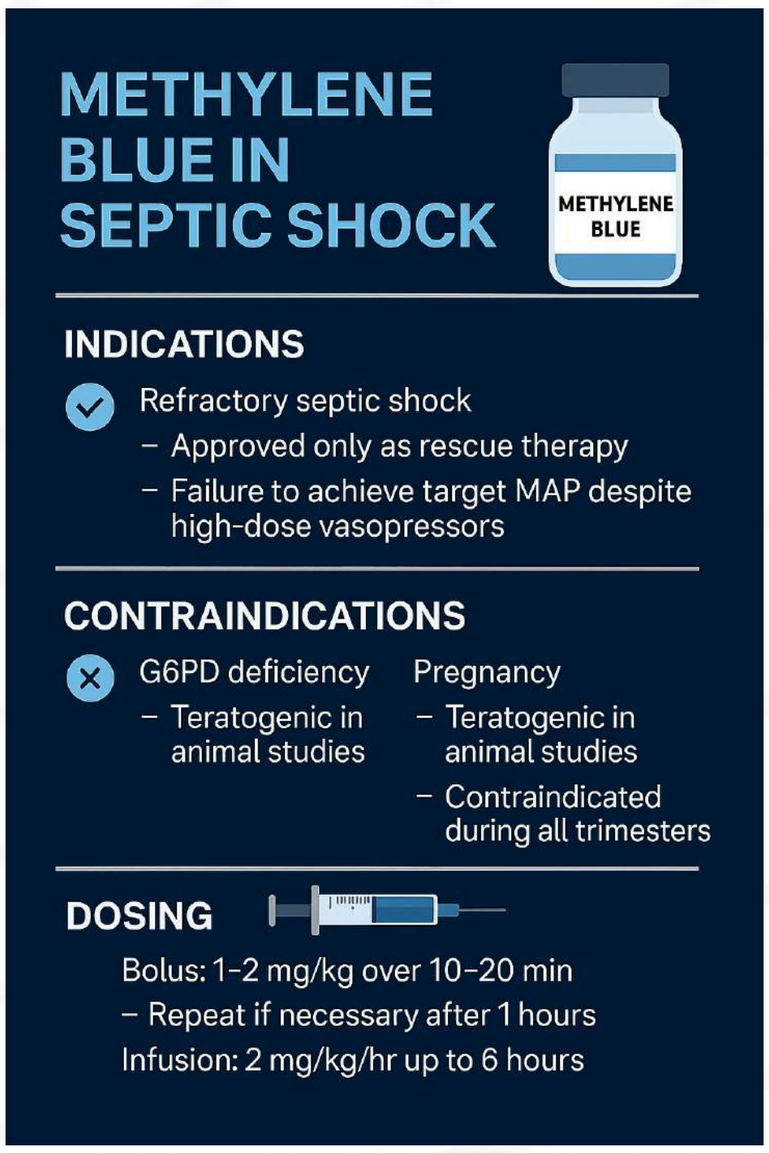

Figure 3: Infographic of methylene blue in shock

Conclusion

This case underscores the potential of methylene blue as a rescue therapy in refractory septic shock complicated by profound vasoplegia, highlighting its role as a promising adjunct when conventional vasopressor strategies are inadequate.

References:
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3. Ibarra-Estrada M, García-Salas Y, Garnica-Garza HM, Padilla-Arellano JR, Ruiz-Beltrán CA, Sánchez-Hurtado LA, et al. Early adjunctive methylene blue in patients with septic shock: randomized controlled trial. Trials. 2024;25(1):339.