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FROM CRISIS TO RECOVERY: LIFE-SAVING IGM-ENRICHED IMMUNOGLOBULIN RESCUE THERAPY IN SEVERE CAP AND REFRACTORY POST-PARTUM SEPTIC SHOCK – A DRAMATIC 24-HOUR TURNAROUND

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The patient expressed appreciation for the comprehensive multidisciplinary care received. During follow-up, she reported complete functional recovery and successful breastfeeding establishment.
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ABSTRACT

Background: Septic shock in the postpartum period is a life-threatening condition associated with significant mortality. The physiological changes of pregnancy and the puerperium often complicate diagnosis and treatment, making timely, effective intervention critical. When conventional antimicrobial therapy fails, alternative therapeutic strategies become essential. Recent systematic reviews have highlighted the potential benefits of IgM-enriched immunoglobulin in reducing mortality among sepsis patients.

Case description: We report the case of a 25-year-old previously healthy woman who developed severe septic shock following caesarean section delivery. The clinical picture was complicated by influenza A pneumonia and a urinary tract infection caused by *Escherichia coli*. Despite administration of broad-spectrum standard antimicrobial treatments, the patient exhibited rapid clinical deterioration, with escalating vasopressor requirements and severe hyperinflammation. Biomarkers were profoundly elevated, including a procalcitonin level of 386.2 ng/ml and a C-reactive protein of 424 mg/l. Given the failure of standard therapy and the critical condition, IgM-enriched immunoglobulin (Pentaglobin®) was administered as a rescue therapy. Within 24 hours of infusion, the patient demonstrated significant clinical and biochemical improvement, with normalisation of vital signs, reduced inflammatory markers and early weaning from vasopressors. She achieved full recovery and rapid hospital discharge.

Conclusion: This case highlights the potential life-saving role of IgM-enriched immunoglobulin and its potential therapeutic value in managing refractory postpartum sepsis and severe community-acquired pneumonia (CAP). While promising, the timing, dosage and patient selection for this therapy require further clinical investigation, particularly in obstetric populations.

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KEYWORDS

Sepsis, community-acquired pneumonia, postpartum sepsis, IgM-enriched immunoglobulin, rescue therapy

LEARNING POINTS

- IgM-enriched immunoglobulin therapy represents a viable adjunctive option for refractory sepsis, particularly in hyperinflammatory presentations. Early therapeutic intervention within 24 hours of refractory status may optimise clinical outcomes.
- Phenotype-based therapy selection can identify patients most likely to benefit from immunomodulatory interventions. Postpartum patients may experience worse outcome due to pregnancy-related immune modifications.
- Biomarker monitoring including procalcitonin and C-reactive protein can guide therapeutic decisions and evaluate treatment response.

INTRODUCTION

Critical illness following childbirth remains a significant healthcare challenge, with sepsis representing a leading cause of maternal mortality worldwide. Maternal sepsis causes an overactive inflammatory response, leading to fluid leakage and intravascular hypovolaemia. In addition, cytokines' release causes a decrease in systemic vascular resistance while simultaneously elevating cardiac output[1].

The immunosuppressive effects of sepsis lead to B-cell dysfunction which results in decreased immunoglobulin production (IgG1, IgA, IgM) mainly among septic shock non-survivors. Bermejo-Martin et al., in a large series of patients with community-acquired sepsis revealed a higher mortality rate of hypoglobulinaemia compared to patients with normal concentrations of IgG1, IgA and IgM. This result supports the potential therapeutic value of IgM-enriched polyclonal immunoglobulin treatment for sepsis[2] as shown *Figure 1* (adapted from Nierhaus et al.[3]).

Additionally, pneumonia occurring in the peripartum period may be more frequent, exhibit atypical features, run a more severe course or be more difficult to treat than in a non-pregnant patient. Also, the postpartum period creates distinctive immunological features through pregnancy-related immune system modifications that can persist after delivery. These alterations may contribute to increased susceptibility to severe infectious complications requiring critical care support[4].

Research studies have investigated the use of immunomodulatory treatments as additional therapy for severe sepsis. Systematic reviews of IgM-enriched

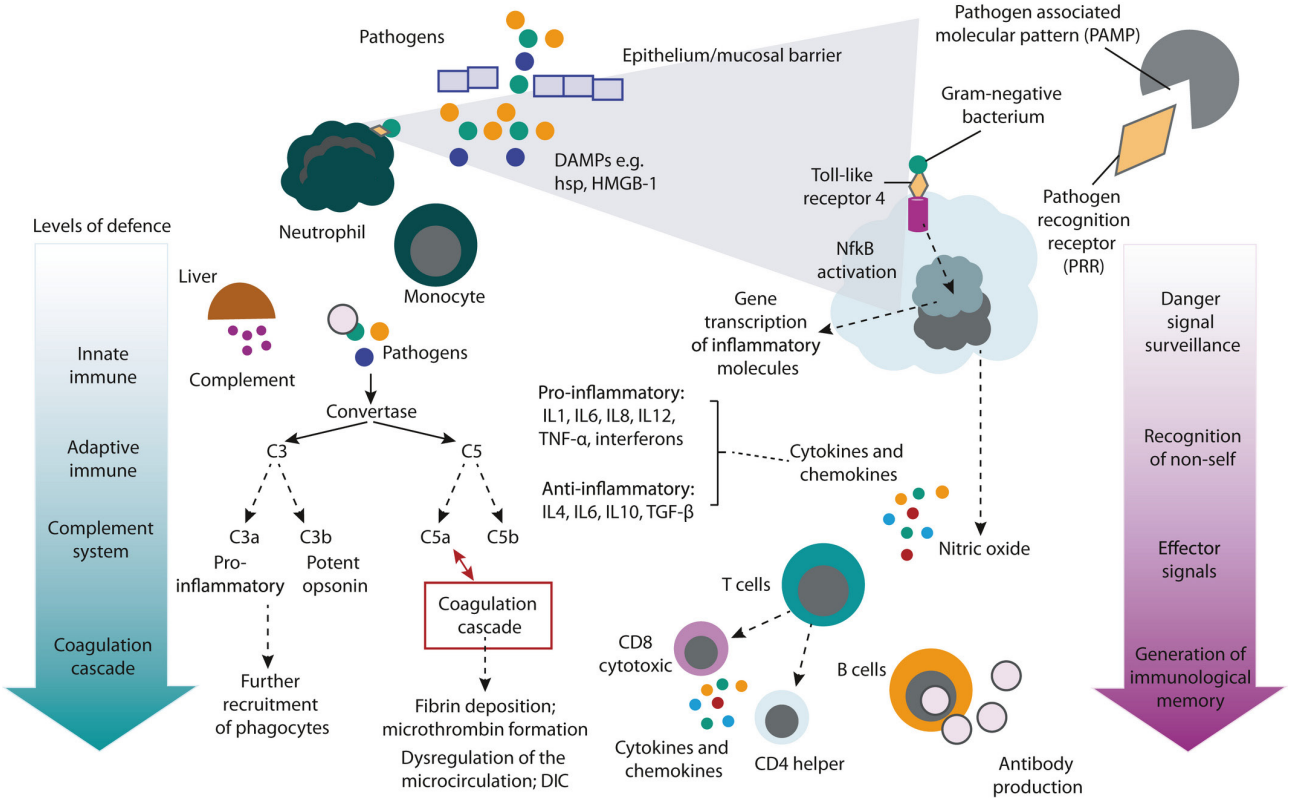


Figure 1. Maternal sepsis pathogenesis: postpartum infection triggers an overwhelming systemic inflammatory response (cytokine storm, endothelial leakage, coagulopathy) culminating in septic shock and organ dysfunction.

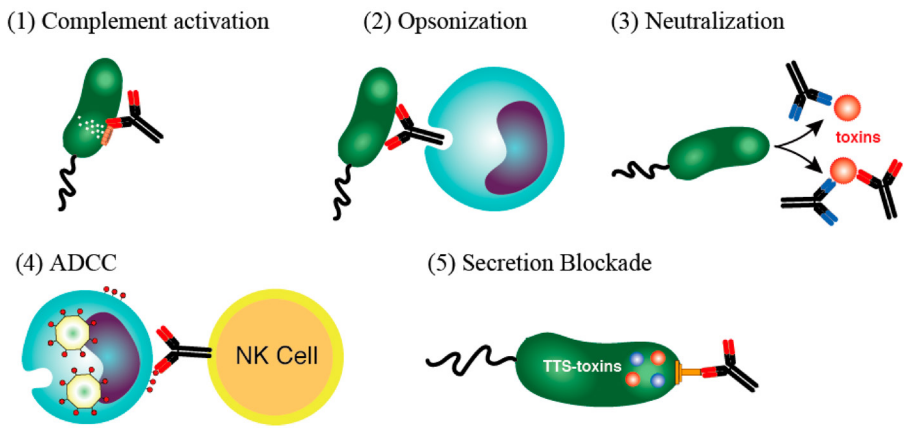


Figure 2. Mechanisms of action of IgM-enriched immunoglobulin (Pentaglobin®) in sepsis: enhanced complement activation, pathogen clearance, toxin neutralization and modulation of inflammation and microcirculation.

immunoglobulin preparations have shown promising results. The research by Cui and colleagues which analysed 19 clinical trials showed that this intervention reduced mortality rates in sepsis patients[5]. Pan and associates discovered that IgM-enriched formulations outperformed standard immunoglobulin preparations in their study[6].

The biological basis of IgM-enriched therapy relies on its superior antimicrobial capabilities. The preparations show better bacterial binding properties and complement activation than standard immunoglobulin products. In addition, in vitro and in vivo models have shown an increase in IL-10 after administration of IgM- and IgA-enriched immunoglobulins as shown *Figure 2* (adapted from Tugrul et al.[7]). The case illustrates how this therapeutic approach can be used in treating a patient who suffered a challenging postpartum sepsis scenario.

CASE DESCRIPTION

A 25-year-old healthy woman in her first pregnancy received regular antenatal care until 40 weeks. She presented to the obstetric clinic for her usual appointment, where she gave a history of respiratory symptoms with productive cough, fever and throat pain starting three days prior to her visit following exposure to individuals with respiratory illness.

Upon admission (day 1), laboratory testing confirmed influenza A infection through a respiratory viral panel. Empirical antimicrobial therapy was initiated with ceftriaxone and metronidazole. Labour induction attempts proved unsuccessful, requiring caesarean delivery.

Post-surgical deterioration (days 2): Following the caesarean delivery, the patient developed progressive respiratory distress characterised by high fever (39°C), rapid breathing (35 breaths per minute), accelerated heart rate (130 beats per minute) and increasing oxygen demands (6–8 litres via a facial mask). These concerning developments prompted intensive care unit transfer for advanced monitoring and support. The patient remained on a continuous high-flow nasal cannula with a flow of 60 l/m and FIO_2 of 60%. A chest X-ray was performed and revealed right lower lobe lung infiltrate with left lower lobe atelectasis *(Fig. 3)*. Escalation of antimicrobial and intravenous hydrocortisone 200 mg/day was started.

Diagnostic workup (day 3): A CT pulmonary angiography scan excluded pulmonary thromboembolism and confirmed bilateral pneumonic patches. Microbiological cultures identified *E. coli* in urine and was sensitive to prescribed antimicrobial agents. Blood cultures were negative. Despite therapeutic escalation including meropenem, clindamycin and vancomycin, clinical deterioration continued with severe hypoxaemia, together with worsening of laboratory parameters. The patient was kept on continuous non-invasive ventilation (bi-level non-invasive ventilation) with high FIO_2 (70%) with pending intubation. Serial biochemical monitoring demonstrated progressive hyperinflammation despite antimicrobial optimisation *(Table 1)*.

Therapeutic intervention (day 4): There was recognition of refractory sepsis with hyperinflammatory characteristics (markedly elevated inflammatory biomarkers exceeding 400 mg/l for C-reactive protein and 380 ng/ml for procalcitonin). The patient's clinical status worsened, including haemodynamic instability requiring vasopressors support, and there was worsening gas exchange suggesting acute respiratory distress syndrome *(Fig. 4)*.

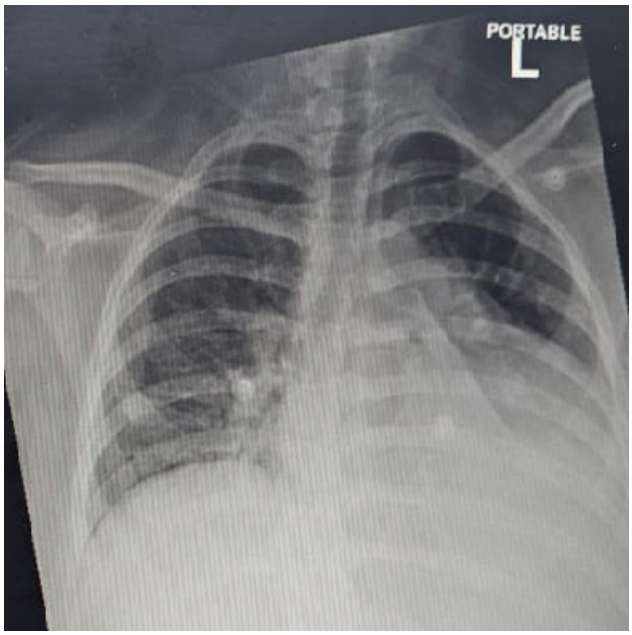


Figure 3. Initial chest X-ray showing mild right lower lobe lung infiltrate with left lower lobe atelectasis.

Laboratory parameter	D1	D2	D3	D4	D5	D6	D7	D8	D10	Normal range
C-reactive protein (mg/l)	-	96	396	424	415	194	131	77	55	<5
Procalcitonin (ng/ml)	0.91	16.5	289.8	386.2	79.2	76.9	35.14	11.5	3	<0.25

Table 1. Daily level of inflammatory markers, C-reactive protein and procalcitonin. Peak values occurred on day 4 (CRP 424 mg/l; PCT 386.2 ng/ml). Following IgM-enriched immunoglobulin therapy initiation, procalcitonin declined from 386.2 ng/ml to 79.2 ng/ml by day 5.

Multidisciplinary teams including intensive care unit (ICU), obstetrics, pulmonology, clinical pharmacy and infectious diseases representatives agreed to initiate IgM-enriched immunoglobulin therapy (Pentaglobin®) at 5 ml/kg daily dosing for three days, following evidence-based protocols for this clinical scenario[8].

Day 5: Clinical response was obvious within one day of immunoglobulin administration. There was a marked improvement of respiratory distress, and temperature normalised from 39°C to 37.8°C. Oxygen requirements decreased from 70% on continuous non-invasive ventilation to 2 litres via a nasal cannula, and procalcitonin declined substantially from 386.2 to 79.6 ng/ml (representing an 80% reduction).

Days 6: Sustained clinical improvement continued: the patient was transferred to intermediate care (day 7), a general ward (day 8) and home discharge (day 10).

A thirty-day follow-up evaluation confirmed sustained recovery with complete symptom resolution and normalised inflammatory biomarkers.

DISCUSSION

This case shows that IgM-enriched immunoglobulin, alongside standard management, can significantly improve severe postpartum sepsis, supporting its use in critically ill patients. IgM-enriched immunoglobulin preparations offer distinct advantages through their unique structural and functional properties. The pentameric molecular configuration enhances complement system activation and antimicrobial effectiveness compared to standard immunoglobulin products. Pentaglobin® contains physiologically representative immunoglobulin distributions (IgM 12%, IgA 12%, IgG 76%) in contrast with conventional preparations that lack IgM components[7,8].



Figure 4. Chest X-ray showing increasing bilateral lung infiltrates suggesting evolving acute respiratory distress syndrome.

Contemporary meta-analyses demonstrate strong evidence for clinical effectiveness. The research by Cui and colleagues showed 40% mortality reduction across multiple studies, with additional benefits including shorter durations of mechanical ventilation[5]. Dinleyici found that paediatric patients experienced an even higher mortality reduction of 59% in their affected population[9]. The treatment of multidrug-resistant bacterial infections has shown specific benefits which lead to major reductions in patient mortality[8].

Current evidence suggests optimal outcomes through phenotype-directed therapy selection. Our patient exhibited classic hyperinflammatory phenotype characteristics in the form of acute onset of haemodynamic instability, markedly elevated inflammatory biomarkers (C-reactive protein >400 mg/l, procalcitonin >380 ng/ml) with poor response to standard therapy. For this phenotype, evidence supports early intervention (within 24 hours) using 5 ml/kg daily dosing for 3–5 days[6].

The linear relationship between therapy initiation and rapid clinical improvement, combined with dramatic biomarker normalisation, suggests genuine therapeutic benefit rather than coincidental recovery. This response pattern aligns with findings from the CIGMA clinical trial, where patients with elevated C-reactive protein demonstrated significant mortality benefits when treated with IgM-enriched immunoglobulin[10].

The treatment did not produce any adverse reactions consistent with favourable safety profiles. The response magnitude and timing of the intervention indicate that the treatment was effective despite the inability of single-case observations to establish definitive causality. There was an inability to definitively attribute improvement to Pentaglobin® versus spontaneous disease resolution. However, the rapid response timeline and huge biomarker changes suggest strong therapeutic benefit rather than natural recovery patterns.

The experience supports current recommendations for multimodal sepsis management which include early source control and careful vasopressor use, and consideration of adjunctive immunomodulatory therapy. The successful outcome supports the implementation of these therapies in treatment protocols for patients who meet specific criteria.

CONCLUSION

This case demonstrates potential therapeutic benefits of IgM-enriched immunoglobulin as rescue therapy for severe CAP and refractory postpartum sepsis. The rapid improvement supports evidence for this intervention in hyperinflammatory sepsis patients.

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