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Using Intravenous Immunoglobulin In a Patient with Septic Shock and Multiple Comorbidities: A Review Based on a Clinical Case

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The review focused on managing sepsis and septic shock patients by administering intravenous immunoglobulins (IVIG). Treatment outcomes and survival prognosis of septic patients were discussed in view of different regimens and dosages of IVIG. The principles of determining the appropriate dosage of IVIG in different medical facilities were compared. Own clinical case of complex treatment of septic shock using IVIG was proposed. The patient experienced a septic shock after transurethral resection of the prostate to treat a prostate abscess. Additionally, the patient was diagnosed with acute cerebrovascular disorder and various cardiovascular ailments, including type 2 diabetes mellitus and stage 2 chronic kidney disease. This septic patient was diagnosed with immunodeficiency disorder with lymphopenia, hypoproteinemia, procalcitoninemia, and significant secondary autoimmune inflammatory disorders. Despite the expected unfavorable prognosis, after comprehensive treatment with early application of moderate doses of IVIG, the patient’s condition stabilized, and organ functions remained satisfactory. Therefore, early administration of intravenous immunoglobulin had a favorable clinical outcome in the treatment of septic shock, thereby indicating the need to utilize a multidisciplinary approach, including involving an immunologist, in managing septic conditions.

Keywords: Sepsis, septic shock, intensive care, intravenous immunoglobulin.
Sepsis is a serious medical and economic issue in the modern world. Sepsis and septic shock are life-threatening conditions caused by the immune system not responding properly to various infections. This causes tissue and organ damage, eventually leading to multiple organ failure and death. Despite significant progress in treatment, sepsis and septic shock remain serious healthcare issues worldwide, resulting in a substantial expenditure of healthcare resources [1,2,3].

Around 30 million cases of sepsis are reported annually around the globe, with 6 million leading to death [4]. Septic shock, which results in multiple organ failure, is the leading cause of death in such patients. Septic shock develops in 40% of patients diagnosed with sepsis, with a mortality rate of 40–80% [5]. The rapid development and innovations of medical diagnostics has led to an exponential growth in the number of patients with multimorbidity conditions worldwide. According to the international definition, multimorbidity determines the simultaneous presence of ≥3 diseases. The occurrence of concomitant pathologies has a detrimental impact on the survival rate of patients suffering from sepsis and septic shock [9]. Sepsis is the most common cause of acute purulent soft tissue infections and post-operative complications. The golden standard of surgical practice in the treatment of prostate abscesses is transurethral resection of the prostate. Despite this treatment method’s apparent effectiveness, it has its drawbacks. As per the findings of a multicenter prospective study conducted in France, it has been determined that 21.6% of patients who underwent transurethral resection of the prostate experienced bacterial complications, with urinary tract infections accounting for 19.3% and septic shock accounting for 2.3% [7,8]. Urosepsis is estimated to account for 9 to 31% of all cases, with a mortality rate of 20–40%. Urologists, specialists in intensive care, and other specialists should all be part of the team that treats sepsis. Immunologists are especially important because sepsis affects the immune system and can lead to secondary immunosuppression with autoimmune inflammatory outcomes. Immunological preparations for intensive therapy, such as immunoglobulins, targeted monoclonal antibodies, growth factors, specific cytokines, etc., are also necessary [9]. These issues are currently undergoing a comprehensive examination and necessitate the expertise of trained specialists [8]. The efficacy of intravenous immunoglobulin administration in patients with septic shock or sepsis was still understudied until recent years [10]. Nonetheless, recent retrospective studies examining the correlation between the administration of intravenous immunoglobulins (IVIG) and favorable outcomes in septic patients with low levels of immunoglobulin G (IgG) in the blood serum have revealed that the application of IVIG in septic patients with low IgG levels in the blood serum is associated with a superior survival prognosis in patients [11,12].

This study aimed to compare the characteristics of this clinical case of septic shock and multiple organ failure with significant immune disorders with the latest global medicine data. Over the past ten years, a comprehensive analysis of published literature has been carried out. The research was conducted using the PubMed database of medical publications from 2013 to 2023. The following MeSH terms were used for the research: “sepsis”, “septic shock”, “comorbid condition”, “intravenous immunoglobulins”, “systemic inflammatory response syndrome.” We have only included accessible full-text sources in the final review. Meta-analyses, review articles, and clinical cases were also included in the analysis.

In total, 2237 publications were found in the PubMed database for the specified period, including 103 full-text sources. Twenty-three sources were selected due to their relation to the chosen problem. Our clinical scenario centered around the use of intravenous immunoglobulin in a patient suffering from septic shock and multiple health conditions. Attention was also given to publications on concomitant pathology in patients with septic conditions.

This review focuses on the contemporary data regarding intravenous immunoglobulin (IVIG) utilization in patients with concurrent severe bacterial infections. In this review, we attempted to summarize the latest evidence regarding the use of IVIG in sepsis and septic shock and to assist clinical physicians in understanding the existing benefits of the potential usefulness of this important therapy in septic shock. According to contemporary literature, the efficacy of intravenous immunoglobulin in the treatment of sepsis or septic shock is contingent upon the type of IVIG preparation employed (either enriched with IgM or with minimal IgM content, IgG), the timing of administration (<24 hours), the dosage, and the inflammatory/immunodeficient profile of the patients [13].

Besides developing new sepsis treatment methods, like microRNA blockers, colony-stimulating factors, cytokines, and monoclonal antibodies, the study of how effective already registered drugs are continues. One of such drugs is intravenous immunoglobulin G – IVIG. Intravenous Ig G is an international name for Human normal immunoglobulin G, the drug, which is an immunologically active protein fraction (ratio of immunoglobulin G
subclasses in the drug: Ig G 1: 43–75%; Ig G 2: 16–48%; Ig G 3: 1.7–7.5%; Ig G 4: 0.8–11.7%). The drug’s active ingredient is antibodies that work against viruses and bacteria, including hepatitis A and B, herpes, chickenpox, influenza, measles, mumps, poliomyelitis, rubella, pertussis, staphylococcus, Escherichia coli, pneumococci, and mycobacterium tuberculosis. The 10% solution for intravenous infusion, 100 ml, manufactured by Biopharma, Ukraine (the Certificate of State Registration of Medical Immunobiological Preparation No. 841/11-300200000 dated June 8, 2011). Immunoglobulin G is used for replacement immunotherapy for primary and secondary immunodeficiency disorders and associated diseases, as well as for treating and preventing diseases caused by bacterial and viral infections.

Immunoglobulins are key effector molecules in the humoral immune response in many serious diseases. Intravenous multivalent immunoglobulin is a preparation of polyclonal serum immunoglobulins, usually IgG, from thousands of donors. It is utilized as an adjunct therapy in critically ill patients suffering from severe infections, such as sepsis, septic shock, and necrotizing soft tissue infections. Since the early 1990s, IVIG has been used to treat patients with severe invasive group A streptococcal infection. IVIG is also widely used to treat necrotizing soft tissue infections. It is also used for various autoimmune, inflammatory neurological, skin, and immunodeficiency diseases, as well as in the case of COVID-19 and reproductive medicine [14,15,16,17]. The meta-analysis of available clinical studies on the use of IVIG in Group A streptococcal toxic shock syndrome indicates benefits in terms of patient survival after severe septic shock [18]. The efficacy of IVIG was assessed in a cohort of 100 individuals in the intensive care unit with necrotic soft tissue infections, including any bacterial etiology, in a placebo-controlled clinical trial (INSTINCT). The study found no adverse effects in the patient’s records on the patients’ lives six months after the administration of IVIG [12].

A retrospective analysis of 646 medical records of surgical patients treated for secondary peritonitis in the intensive care unit was conducted in another study. Clinical data of patients were assessed using the SOFA scale upon admission, and their changes in sequential organ failure assessment were analyzed during a 7-day hospitalization cycle in this department to confirm sepsis and delta neutrophil index (DNI). The mortality of patients with septic shock was evaluated. The scores were given based on susceptibility to sepsis during comparative analysis in the IVIG group and the group without IVIG. It has been determined that the use of IVIG was significantly associated with a faster decrease in DNI, which means a faster reduction of inflammation. As the immune system responds rapidly, it is feasible to consider administering intravenous immunoglobulin after the surgery to manage the source in patients suffering from abdominal sepsis, particularly those with weakened immunity [19].

During a septic process, the delicate systems of innate and acquired immunity, inflammation, and anti-inflammatory processes are disrupted in various ways. Pro-inflammatory and anti-inflammatory pathways and the coagulation and complement cascades are activated. These patients are at risk of developing severe immunodeficiency disorder with lymphopenia and hypogammaglobulinemia (D84.8 according to ICD-10) caused by sepsis. The administration of intravenous immunoglobulin is one of the most prominent adjunctive treatments investigated and administered in patients with sepsis. Immunoglobulin preparations for intravenous administration have several mechanisms of action, such as neutralizing antigens, blocking Fc receptors on phagocytic cells, changing cytokine responses, and modulating immune cell functions. Thanks to various interactions in this network, high doses of IVIG are used, some enriched with IgM, others with only IgG, which is a promising therapeutic approach [20]. The tactic was aimed at pure anti-inflammatory therapy, which had a positive effect, especially with IgM. Studying ways to regulate the immune system, specifically IgG production, seems to be a more apt approach for IgG preparations. Considering their numerous effects on both immune-inflammatory and autoimmune mechanisms, the use of polyclonal intravenous immunoglobulins presents a promising approach for regulating both pro- and anti-inflammatory pathways, particularly those that are immunoregulatory. However, further clinical studies are needed to substantiate the appropriateness of using different immunoglobulins in the targeted group of patients at the early stage of sepsis and septic shock, in the appropriate dosage and for the optimal duration [21,22]. The efficacy of intravenous immunoglobulin in critically ill patients with COVID-19 who required extracorporeal membrane oxygenation was studied. About 44% (15/34) of patients had Group A Streptococcus or Panton-Valentine Leukocidin produced by S. aureus. The use of IVIG in these patients was safe. The mortality rate was 30% lower compared to other studies, with a predicted mortality rate of >90% based on the Sequential Organ Failure Assessment (SOFA) score [23].

Toxic shock syndrome (TSS) is a rare complication of an infection caused by streptococci and staphylococci. This condition is associated with a high mortality rate in these patients. When assessing these patients with symptoms of shock and skin infection foci or soft tissues, it is crucial to consider that a high percentage of these patients will
develop a septic condition. The survival of these patients is improved by rapid diagnosis and comprehensive treatment with surgical intervention, antibiotics, hemodynamic stabilization, and adjuvants, such as IVIG [24]. When toxic shock syndrome is caused by streptococcal infection, IVIG is administered at doses of 2 g/kg of body weight in a single daily dose during the initial days of shock onset [25]. According to Atlantic recommendations for treating toxic shock syndrome, the dosage should be 1 g/kg on day one and 0.5 g/kg on days 2–3 or 0.15 g/kg per day for five days [26].

In a separate study, the utilization of intravenous immunoglobulins in patients admitted to intensive care units was examined. The outcome was assessed by comparing the patients who survived the treatment with those who died after the treatment. The levels of evidence confirming the use of IVIG, the schemes of their prescription, and the costs were determined. The intravenous administration of immunoglobulin is prescribed for many indications in the intensive care unit, with various dosing regimens. The results of clinical trials have shown that patients who survived hospital admissions received higher and larger doses of intravenous immunoglobulin than those who did not, as confirmed by other meta-analyses. The optimal dosage of IVIG administration is 1.5-2 g/kg of body weight per day [27,28,29]. In the clinical protocol for providing specialized care at the hospital stage to patients with sepsis or septic shock in Ukraine, the authors also recommend using high doses of immunoglobulin in sepsis (2 g/kg of body weight per day) [30].

Japanese researchers recommend the following IVIG administration schemes for treating severe infections covered by Japanese medical insurance. The first scheme involves taking 5g/day for three days. The second scheme involves a single dose of 15g within one day. Moreover, the second scheme for treating sepsis, which presupposes a one-time administration of 15g of IVIG during one day, has shown improvement in the condition and inflammation earlier than the divided administration of IVIG [31].

Sepsis and sepsis-related multiple organ failure are the leading causes of mortality in intensive care units. A single-center, interventional study revealed the effects of intravenous immunoglobulin G (IVIG G) on various types of immunoglobulins and anticoagulant factors in patients with sepsis. This study researched patients with sepsis, severe sepsis, or septic shock from August 2008 to March 2013. The study’s findings indicated that the administration of IVIG G resulted in an elevation of IgM and protein C levels in the serum of the patients. In contrast, a decrease in tissue plasminogen activator-1 (tPAI) levels was observed. It has potential applications for preventing sepsis-induced coagulopathy and disseminated intravascular coagulation [32].

Clinical and experimental evidence shows that IVIG has strong anti-inflammatory and immune-regulatory properties and an etiologic anti-infective effect. Its specific effect is caused by a small amount of always-present antibodies. Nonspecific – with an immunomodulatory effect. Recent achievements in understanding the mechanism of IVIG, where both effects are typically mediated through leukocyte Fc receptors, have been analyzed. Immunoglobulins activate leukocytes by binding with Fc receptors, triggering processes like phagocytosis. Immunoglobulin molecules can opsonize bacteria and neutralize viruses [33]. IVIGs are also capable of actively inhibiting the activation of monocytes, macrophages, dendritic cells, neutrophils, and natural killers by binding to Fc-gamma receptors, neutralizing activated components and the membrane-attacking complex of the complement system, and modeling functions of B-cells and plasma cells, regulating the T-cell balance between Treg cells and effector T-cells (for example, Th1, Th17), reducing the production of pro-inflammatory cytokines (INF-α and INF-γ, TNF-β, interleukins 1, 2, 3, 6, 9, 11, 12, 38), which cause hyperinflammation, also known as “cytokine storm” – an autoimmune inflammatory complication [11,21].

Thus, the use of systemic immune modulators, such as IVIG, can prevent an abnormal immune response, a hyperergic inflammatory response with autoimmune consequences observed in septic conditions [21].

**Clinical case**

On May 26, 2022, a 53-year-old patient, F. (born on October 27, 1968), was admitted to the Department of Anesthesiology and Intensive Care (DAIC) of the “First Territorial Association of Lviv” Detached Subdivision “Hospital of St. Panteleimon” with the preliminary primary diagnosis of post transurethral resection of the prostate (TUR) and drainage of the prostate abscess. Patient’s accompanying diagnoses: Ischemic heart disease (IHD). Diffuse coronary atherosclerosis. Paroxysm of atrial fibrillation since May 26, 2022. Hypertensive disease stage III, grade 2, risk 4. CH IIa. The condition after a recent acute cerebrovascular event (ICE) on March 2, 2022. Right-sided hemiparesis, motor aphasia. Type 2 diabetes in the stage of subcompensation, insulin-dependent with generalized
angiopathies: retinopathy, angiopathy of the lower extremities, encephalopathy. Chronic kidney disease (CKD) 2nd stage: glomerulosclerosis, urolithiasis, chronic renal insufficiency stage II.

According to the medical history, the patient has been ill for several days. He noticed elevated body temperature, 38 °C, general weakness, and discomfort in the urethra due to the Foley catheter’s presence. Due to the acute cerebrovascular event and the patient’s inability to urinate independently, a Foley catheter has been inserted for an extended time.

The patient consulted the emergency department of the “First Territorial Association of Lviv” Detached Subdivision “Hospital of St. Panteleimon.” At the admissions department, he underwent a computerized tomography of the abdominal cavity organs (CT of the AC): Benign hyperplasia and a prostate gland abscess were diagnosed.

The urologists at the clinic have reached a decision to perform a scheduled surgical procedure on May 26, 2022, namely endoscopic prostate resection and abscess drainage. Duration of the procedure: 45 min. Anesthesia: intravenous with an adequate supply of oxygen and infusion therapy.

The patient’s general condition deteriorated rapidly in the initial post-operative period. Consciousness was a superficial stupor, gradually transitioning into a deep one. Hemodynamics was unstable: heart rate (HR) 140/min, arterial blood pressure (BP) 80/40, body temperature 39 °C. On auscultation, breathing was hard and weak in the lower part of the lungs. The breathing rate (RR) was 23 breaths per minute. The skin and mucous membranes were pale, covered in cold sweat. The decision was made to transfer the patient to the Department of Anesthesiology and Intensive Care.

During the initial objective examination conducted at the Department of Anesthesiology and Intensive Care, the following findings were established: the general condition – severe; the patient’s consciousness – profound stupor. The pupils are symmetrical; light reflexes are weak. Pale skin and mucous membranes. Respiratory system: On auscultation, breathing is harsh, weakened in the lower lobes bilaterally, RR 24/min, SpO2 96%, oxygen therapy is administered via a non-rebreather mask at 6 L/min. Cardiovascular system: hemodynamics is unstable, pulse 140/min, blood pressure 80/40, heart sounds are muffled and rhythmic on auscultation. Body temperature is 39 °C. Neurologically: right-sided hemiparesis, motor aphasia.

The DAIC has set monitoring of vital functions, blood samples were collected for laboratory testing, central venous catheterization was performed, echocardiography, chest X-ray, arterial blood gas analysis, and consultations with related specialists, including a cardiologist, functional diagnostics physician, and urologist, were requested. Urgent intensive therapy was initiated.

Cordarone was given intravenously (IV) to stabilize hemodynamic parameters: bolus 300 mg and 450 mg for the next 4 hours. Norepinephrine was infused at 0.02 mcg/kg/min, and potassium-enriched electrolyte solution was administered intravenously. Paroxysm of atrial fibrillation from May 26, 2022, transformed into sinus rhythm.

After stabilizing the patient’s condition to exclude the presence of damage to various organs and systems, a series of instrumental examinations were performed: electrocardiography. Conclusion: atrial flutter; X-ray of the chest. Conclusion: No visible focal infiltrating changes. The sinuses are clear. Post-inflammatory fibrotic changes in the right cardio diaphragmatic angle; echocardiogram. Conclusion: The size of the heart is within normal limits. Hypertrophy of the left ventricle walls: The aorta is not dilated, it is hardened. Degenerative changes in heart valves. Left ventricular myocardial contractility is satisfactory: Ejection fraction – 55%. Hypokinesia of the apex of the left ventricle, lateral wall. Fluid in the pleural cavity is not visualized. Ultrasound examination of the abdominal cavity (Abdominal Ultrasound): Chronic left-sided pyelonephritis.

Laboratory tests performed: A complete blood count with a differential leukocyte count and erythrocyte sedimentation rate, biochemical blood analysis, coagulogram, C-reactive protein, procalcitonin, blood lactate, and procalcitonin (see Tables 1–4 for indicator dynamics).
Table 1. The dynamics of clinical blood count in septic condition

<table>
<thead>
<tr>
<th>Date/value</th>
<th>WBC ($10^9$/l)</th>
<th>(4–9)</th>
<th>RBC ($10^3$/l)</th>
<th>(4–6.2)</th>
<th>HGB (130–160 g/l)</th>
<th>PLT (150–400 10^9/l)</th>
<th>GRA (30–70%)</th>
<th>LYM (20–20%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>May 28</td>
<td>49.16</td>
<td>2.95</td>
<td>84</td>
<td>213</td>
<td>94</td>
<td>1.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>June 7</td>
<td>4.29</td>
<td>2.97</td>
<td>85</td>
<td>188</td>
<td>80.2</td>
<td>14.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>June 21</td>
<td>6.0</td>
<td>3.42</td>
<td>97</td>
<td>320</td>
<td>67.1</td>
<td>26.3</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Changes in values are highlighted in bold black font.

Table 2. The dynamics of biochemical blood test in septic condition

<table>
<thead>
<tr>
<th>Date/Value</th>
<th>Total Protein (64–83 mmol/L)</th>
<th>Albumin (36–49 g/L)</th>
<th>Bilirubin total (&lt;18.7 micromoles/liter)</th>
<th>Calcium (1.16–1.32 mmol/L)</th>
<th>Glucose (4.1–5.9 mmol/L)</th>
<th>Urea (3.8–8.3 mmol/L)</th>
<th>Creatinine (&lt;0.106 μmol/L)</th>
<th>AST (&lt;37 U/L)</th>
<th>ALT (&lt;41 U/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>May 28</td>
<td>56.2</td>
<td>37.1</td>
<td>12.7</td>
<td>1.99</td>
<td>8.85</td>
<td>7.7</td>
<td>85</td>
<td>12</td>
<td>15</td>
</tr>
<tr>
<td>June 12</td>
<td>52.4</td>
<td>46</td>
<td>17.0</td>
<td>2.5</td>
<td>4.6</td>
<td>2.10</td>
<td>65</td>
<td>18</td>
<td>21</td>
</tr>
<tr>
<td>May 21</td>
<td>55.8</td>
<td>48</td>
<td>14.6</td>
<td>2.33</td>
<td>6.10</td>
<td>5.10</td>
<td>67</td>
<td>13</td>
<td>15</td>
</tr>
</tbody>
</table>

* Changes in values are highlighted in bold black font.

Table 3. Dynamics of acute phase blood indicators in septic condition

<table>
<thead>
<tr>
<th>Date/Value</th>
<th>C.R.P. (0–5 mg/mL)</th>
<th>ESR (1–10 mm/hour)</th>
<th>Procalcitonin ng/mL</th>
<th>(0–0.05)</th>
<th>Lactate mmol/L</th>
<th>(0.5–2.2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>May 27</td>
<td>54</td>
<td>47</td>
<td>110</td>
<td>5.9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>June 8</td>
<td>168</td>
<td>113</td>
<td>2.07</td>
<td>1.8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>July 27</td>
<td>36</td>
<td>20</td>
<td>0.61</td>
<td>0.9</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Elevated values are marked in bold black font.
Table 4. Dynamics of coagulogram values in septic condition

<table>
<thead>
<tr>
<th>Date/Value</th>
<th>Prothrombin time (15–17”)</th>
<th>PT (80–105%)</th>
<th>PTT (24–34)</th>
<th>TT (15–22s)</th>
<th>INR (0.8–1.2)</th>
<th>Fibrinogen (2–4 g/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>May 27</td>
<td>15.4</td>
<td>69.7</td>
<td>31</td>
<td>22.3</td>
<td>1.30</td>
<td>3.90</td>
</tr>
<tr>
<td>June 7</td>
<td>11.26</td>
<td>96.0</td>
<td>35</td>
<td>14.10</td>
<td>1.0</td>
<td>3.60</td>
</tr>
<tr>
<td>June 21</td>
<td>13.10</td>
<td>84.2</td>
<td>28</td>
<td>16.6</td>
<td>1.10</td>
<td>2.90</td>
</tr>
</tbody>
</table>

* Changes in values are highlighted in bold black font.

A study of myocardial necrosis markers was also conducted: troponin I: 0.1 ng/mL (the normal range is 0.1-0.16 ng/mL). Blood and urine tests were performed for sterility.

Results of the microbiological study of urine received on May 27, 2022: *E. coli* 10^4, *Klebsiella pneumoniae* 10^5 in the blood is sensitive to Polymyxin B, Gentamicinum, Amikacinum, Ceftazidime.

The results of the microbiological blood test received on June 2, 2022: *Klebsiella pneumoniae* 10^5 in the blood is sensitive to Polymyxin B, Gentamicinum, Amikacinum, Colistin, and Tigecycline.

Based on the disease history (prostate TUR due to prostate abscess), clinical findings (body temperature of 39 °C, decreased blood pressure, tachycardia, tachypnea), and laboratory data (elevated C-reactive protein, procalcitonin, and serum lactate, lymphopenia, hypoproteinemia, bacterial infection in blood culture), the patient’s diagnosis of septic shock with immunodeficiency disorder has been confirmed – A48.3 in ICD-10 with D84.8 in ICD-10.

The patient was admitted to the intensive care unit for an ultrasound examination of the lower limb vessels, which revealed the presence of atherosclerosis in the lower limb arteries. Stenosis of both tibial segments of the lower extremities. There was no evidence of thrombosis in the deep/superficial veins of the upper extremities, and computed tomography of the abdominal cavity and thoracic organs with contrast revealed insignificant fluid presence in both pleural cavities. Residual post-inflammatory changes in the lower part of the right lung. Post-operative changes of the prostate, condition after transurethral resection of the prostate abscess. Right kidney concrements. Additional endoscopic insertion of a urinary stent was performed.

To eliminate anemia, a decision was made to transfuse erythrocyte mass and whole blood. A few days later, urologists performed a percutaneous cystostomy and stenting of the right kidney and ureter.

While in the DAIC, the patient received modern etiotropic and pathogenetic treatment: adequate infusion therapy (balanced crystalloids, colloids (20% albumin)); hemothransfusion therapy (transfusion of erythrocyte mass and whole blood immediately after admission to the DAIC); antibiotic therapy (Levofloxacin 750 mg/day, Ceftazidime 1 g twice a day on May 26, 2022. On May 27, 2022, the antibiotic therapy was changed to Meropenem 1 g three times a day, Amikacinum 1 g once a day); intravenous immunoglobulins (Bioven 10%) at a dose of 100 mL intravenously – 0.5 mg/kg for 30 minutes – 5 g per day for five days from May 29 to June 3, 2022; insulin therapy 24 units per day, at a rate of 1 unit/hour; anti-ulcer therapy (Omeprazole – 20 mg/day); Rapid initiation of enteral nutrition in the early days of intensive care.
Table 5. Dynamics of internal organ values in septic condition

<table>
<thead>
<tr>
<th>Date</th>
<th>Overall condition</th>
<th>Consciousness</th>
<th>Respiratory system</th>
<th>Cardiovascular system</th>
<th>GI tract</th>
<th>Urinary system</th>
</tr>
</thead>
<tbody>
<tr>
<td>May 27</td>
<td>Severe</td>
<td>Coma I</td>
<td>Oxygen therapy SpO2-97% RR – 20 breaths per minute</td>
<td>The hemodynamics is unstable, Ps 100 bpm, BP 100/60 mmHg.</td>
<td>Soft, non-painful stomach.</td>
<td>Urine is hemorrhagic, 6300 ml/day through a catheter.</td>
</tr>
<tr>
<td>June 6</td>
<td>Severe</td>
<td>Clear</td>
<td>Breathing is independent, respiratory rate - 16 per minute.</td>
<td>Hemodynamics is stable, Ps 90 beats per minute, BP 120/80 mmHg.</td>
<td>Soft, non-painful stomach.</td>
<td>The urine is dark, 4100 mL/day via a catheter.</td>
</tr>
<tr>
<td>June 21</td>
<td>Moderately severe</td>
<td>Clear</td>
<td>Breathing is independent and adequate, with a respiratory rate of 14 breaths per minute.</td>
<td>Hemodynamics is stable, Ps 80 bpm, BP 120/80 mmHg.</td>
<td>Soft, non-painful stomach.</td>
<td>Urine is yellow, 2500 ml per day, independently.</td>
</tr>
</tbody>
</table>

On June 21, 2022, the patient was moved to a rehabilitation facility for rehabilitation treatment due to considerable condition improvement. At the time of transition, consciousness was clear. Breathing is independent and adequate. Hemodynamically stable. The stomach is soft. Eats without assistance. The rate of diuresis is sufficient.

The described clinical case intrigued us with its complicated course, the presence of septic shock, multiple comorbidities, and the early use of IVIG in the early stages of sepsis. This case was complex in terms of the prognosis for the patient’s survival.

The patient received intravenous immunoglobulin because of the presence of a severe immune deficiency disorder with sepsis and septic shock, which was confirmed by lymphopenia and low protein levels. This immunodeficiency was accompanied by an autoimmune inflammatory process known as a “cytokine storm”, which can be inferred indirectly from elevated levels of procalcitonin, C-reactive protein, and ESR. In the complex treatment, it was recommended to use average doses of IVIG due to the presence of stage II CKD.

The clinical effectiveness of IVIG in this multi-comorbid patient was made possible by its ability to act as an anti-inflammatory, immunoregulatory, and substitutional agent. Consequently, signs and symptoms of acute distress syndrome dissipated, decreasing the severity of the respiratory failure. The current severe form of bacterial-toxic infection caused by surgical complications, accompanied by septic bacteremia and septic shock, calls for a dose of IVIG of 2 g/kg, subject to preserved kidney function.

In conclusions: Currently, the mechanisms of action of high doses of IVIG represent a highly valuable treatment option for a diverse range of severe immunopathological syndromes in patients with autoimmune and immune-inflammatory diseases, as well as after organ and cell transplantation, which are unresponsive to conventional therapy. A consultation with an immunologist in a multidisciplinary team is also needed to make a complete immunological diagnosis and prescribe pathogenic therapy. It can be concluded that early diagnosis, timely initiation of intensive therapy, and the use of intravenous immunoglobulin G in complex patient management have significant potential in treating comorbid patients with septic conditions. This approach can be used to save lives and reduce mortality in case of sepsis.
References


