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Successful IgM-enriched immunoglobulin treatment in severe COVID-19 pneumonia: a case report

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Abstract

Coronavirus disease (COVID-19) pandemic has turned into one of the most considerable challenges worldwide. The optimal treatment strategy, particularly in severely ill patients, is still unrecognized. IgM-enriched immunoglobulin (Pentaglobin®, Biotest AG, Dreieich, Germany) contains IgM, IgA and IgG against a variety of pathogens representing passive immune protection for affected individuals and it may be effective in the treatment of COVID-19. On March 16, 2020, a 32-year-old woman presented to Masih Daneshvari Hospital, Tehran, Iran. On admission, the peripheral oxygen saturation (O2 Sat) was 84%. Spiral chest computed tomography (CT) scan revealed bilateral ground-glass opacification (GGO) involvement. On March 19, 2020, the clinical condition was deteriorated, and her O2 Sat decreased to 70% in ambient air. Treatment with IgM-enriched immunoglobulin was immediately initiated over the course of three days (total dose for the patient was calculated to be 1500 ml). On the seventh day of hospitalization, the patient was discharged with satisfactory general condition, without any complaints, and with stable vital signs and O2 Sat of 95% on room air. In conclusion, IgM-enriched immunoglobulin could be considered as a potential option for the treatment of severely ill patients with COVID-19.

Key word: IgM-enriched immunoglobulin (Pentaglobin), Coronavirus disease (COVID-19), Acute respiratory distress syndrome (ARDS).

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Introduction

Coronavirus disease (COVID-19) pandemic caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) has turned into one of the most considerable challenges worldwide (1). Cytokine storm is one of the most life-threatening complications in COVID-19 infection. Several immune-active molecules and pro-inflammatory cytokines are shown to contribute to this condition which consequently leads to acute respiratory distress syndrome (ARDS) and multi-organ failure. Furthermore, patients who develop a more severe COVID-19 infection and require intensive care unit (ICU) admission are shown to have higher concentrations of proinflammatory mediators compared to non-ICU patients (2).

It has been suggested that in SARS-CoV-2 infection, inhibition of the uncontrolled over-production of inflammatory markers and modulating the immune response could be associated with reduced mortality (3).

IgM-enriched immunoglobulin contains IgM, IgA and IgG against a variety of pathogens providing passive immune protection for affected individuals. The precise mechanism of action of immunoglobulin therapy remains unclear. However, various mechanisms have been proposed, including neutralizing endotoxin activity, lowering inflammatory gene expression, and directly scavenging inflammatory molecules (4).

The use of hyperimmune globulin has demonstrated clear effectiveness in the treatment of SARS-CoV-2 and the Middle East respiratory syndrome (MERS) corona virus infections, but its therapeutic benefit on COVID-19 pneumonia is still under debate (5). In this study the effect of IgM-enriched immunoglobulin in the treatment of severely ill patients with

COVID-19 has been evaluated.

Case Presentation

On March 16, 2020, a 32-year-old woman presented to the emergency department of Masih Daneshvari Hospital, Tehran, Iran, with shortness of breath and dry cough on exertion. The patient had no underlying diseases and history of medicine usage, except the history of fever, dry cough, myalgia, headache and shortness of breath started one week before presentation and lasted for three days. Emergency management services (EMS) examination showed no need for more evaluation. She was advised on symptomatic treatment and being quarantined at home. These symptoms worsened rapidly after 3 days of illness, despite receiving the supportive care according to the patient's need (acetaminophen for fever, myalgia and headache, and antitussive for dry cough).

On examination, the peripheral oxygen saturation (O2 Sat) was 84%. Other vital signs, including blood pressure, respiratory rate, heart rate and temperature, are shown in table 1. Hypoxia was corrected by oxygenation with facemask (2-4 lit/min). Moreover, on admission, laboratory measures suggested the massively elevated C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR). No other abnormality was found in his laboratory biomarkers (Table 1).

Table 1

Laboratory findings of the patient on admission

Variable	
Vital signs	
Temperature (°C)	37.2
Heart Rate (beats/minute)	130
Respiratory Rate (breaths/minute)	24
Blood Pressure (mmHg)	130/80
O2 Sat (%)	84
Complete Blood Count	
White blood cells (× 10^3 cells/µL) (normal range 4–11)	4.4
Lymphocyte (%) (normal: 34%)	53
Hemoglobin (g/dL) (normal range 12.3-15.3)	13.4
Platelet (× 10^3 cell/µL) (normal range 150-450)	239
Blood biochemistry	
Blood urea nitrogen (mg/dL) (normal range 10-50)	31
Serum creatinine (mg/dL) (normal range 0.6-1.1)	1.1
Aspartate aminotransferase (IU/L) (normal range 5–40)	40
Alanine aminotransferase (IU/L) (normal range 5–40)	38
Coagulation function	
D-dimer (ng/mL) (normal range <500)	280
Infection-related biomarkers	
C-reactive protein,(mg/L) (normal range <10)	8
Erythrocyte sedimentation rate (mm/h) (normal range <30)	76
Inflammatory mediators	
Interleukin 6, pg/mL (normal range up to 59)	12.5

Spiral chest computed tomography (CT) scan revealed bilateral ground-glass opacification (GGO) involvement (Figure 1).

The patient received initial therapy with ceftriaxone 1 g twice daily, azithromycin 500 once daily and intravenous (IV) fluids.

The patient's swab specimen was tested positive for COVID-19 by reverse transcription polymerase chain reaction (RT-PCR) on March 18, 2020 (cycle threshold value 22.39).

On March 19, 2020 the clinical condition was deteriorated, and her O2 Sat decreased to 70% in ambient air. The hypoxia was corrected by reservoir bag (8-10 lit/min) until O2 Sat reached 85%.

Ethics Committee approval and written informed consent have been obtained (Ethics committee reference number: IR.SBMU.NRITLD.REC.1399.014). Treatment with IgM-enriched immunoglobulin (Pentaglobin®, Biotest AG, Dreieich, Germany) was immediately initiated over the course of three days (patient's body weight ~100 kg).

According to the dosing scheme of IgM-enriched immunoglobulin provided in the package information leaflet, a total 3-day dose for the patient was calculated to be 1500 ml. The first 100 ml of IgM-enriched immunoglobulin was administered via IV infusion at the rate of 0.4 ml/kg/h, while the remaining dose was administered by the infusion rate of 0.2 ml/kg/h. On the second day of IgM-enriched immunoglobulin treatment, room air O2 Sat was 90%. Following the second dose, O2 Sat was increased to 94%. After the three-day treatment period, the patient's general condition and O2 Sat were improved and the chest discomfort was well reduced.

On the seventh day of hospitalization, the patient was discharged with satisfactory general condition without any complaints, and with stable vital signs and O2 Sat of 95% on room air.

Discussion

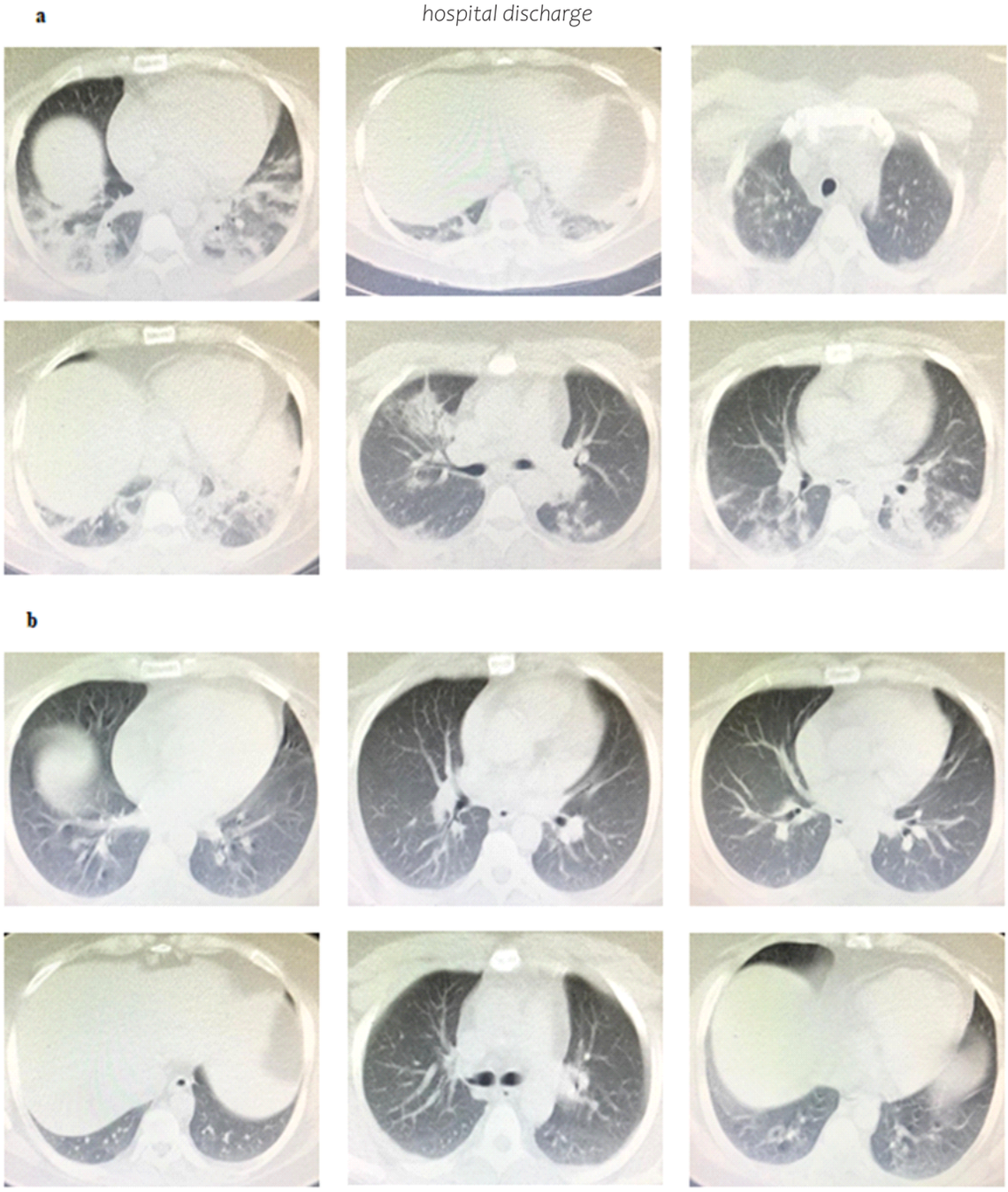
We presented a case of severely ill COVID-19 in whom IgM-enriched immunoglobulin administration showed the acceptable improvement of clinical outcomes.

A number of studies demonstrated that coronavirus infection induces virus-neutralizing antibodies and therefore, convalescent plasma therapy may play an important role in host defense against both SARS (6) and MERS infections (7). Various inflammatory markers were linked to SARS-CoV-2 loads, which were associated with COVID-19 induced ARDS. Moreover, patients who develop a more severe COVID-19 infection and require intensive care unit (ICU) admission are shown to have higher concentrations of proinflammatory mediators than those not requiring ICU. Thus, cytokine storm might play a crucial role in severity of the disease (2, 8).

Previous studies that compared clinical efficacy of

Figure 1

(a) Chest computed tomography scan of patient on admission. (b) Chest computed tomography scan of patient two weeks after hospital discharge



standard IVIg with an IgM-enriched IVIg in different cases revealed that the inhibitory capacity of the IgM-enriched IVIg preparation was evidently higher than that of the standard IVIg (9).

In the current study, we explored the effect of IgM-enriched immunoglobulin on the improvement of the clinical symptoms, laboratory examination and prognosis of the patient's condition.

Administration of IgM-IVIg, as adjuvant therapy, in adult septic patients may be associated with shortened duration of mechanical ventilation and reduced mortality due to modulating both pro- and anti-inflammatory processes (10, 11). Likewise, another study reported positive effect of IgM-IVIg on muscular microcirculation in septic shock (12). In a study conducted by Wand and et al, on 26 patients with severe sepsis or septic shock, level of endotoxin activity could significantly be reduced following 6 and 12 hours of IgM-enriched immunoglobulin administration (13).

One study which compared neutralizing antibody with IVIg, showed that neutralizing antibody can stop viral replication through blocking the receptor binding, preventing the virus from further damaging the target cell, or preventing uncoating of the virus once inside the cytoplasm (5).

Another study that was done on twelve SARS patients whose condition continued to deteriorate despite corticosteroid and ribavirin therapy, showed that IgM-

enriched immunoglobulin, as a safe and effective option, could significantly improve oxygenation in steroid-resistant SARS (14).

In this case, we evaluated the therapeutic efficacy and safety of IgM-enriched immunoglobulin in patients with severe COVID-19 pneumonia. The results showed that IgM-enriched immunoglobulin might result in reducing the disease severity and improving the clinical symptoms. This result was supported by the lung CT scan that showed dramatic response to IgM-enriched immunoglobulin treatment. Regarding safety concerns, no significant adverse drug reaction was noted in this study.

In conclusion, IgM-enriched immunoglobulin could be considered as a potential option for the treatment of COVID-19 pneumonia through modulating excessive inflammatory responses.

Data Availability

All data generated and analyzed during the study are included in the published article and can be shared upon request.

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None.

Author contribution

Farzaneh Dastan: Conceptualization, Methodology, Writing – Review & Editing, Formal Analysis. **Golnaz Afzal**: Methodology, Writing – Original Draft Preparation. **Somayeh Ghadimi**: Methodology. **Hamidreza Jamaati**: Methodology. **Raha Eskandari**: Writing – Review & Editing. **Mohammad Farzad Nazari**: Methodology. **Sahar Yousefian**: Methodology. **Seyed Mohammad Reza Hashemian**: Methodology. **Ali Amir Savadkoohi**: Methodology. **Payam Tabarsi**: Writing – Review & Editing.

Conflicts of Interest

The authors declare no conflict of interest.

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